

The Mre11/Rad50/Nbs1(Xrs2) complex and DNA double-strand break processing

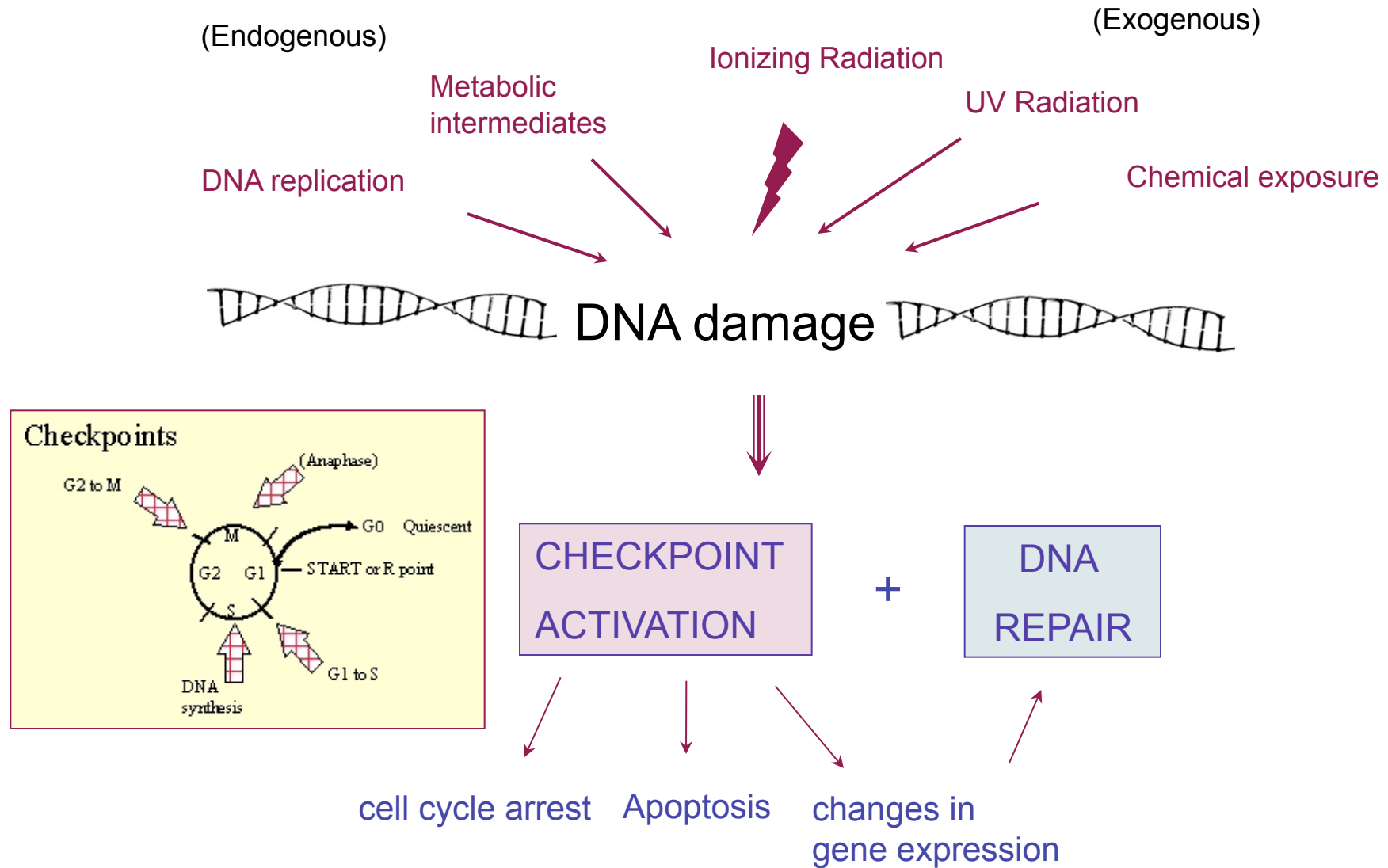
1. archaea
2. budding yeast

Tanya Paull

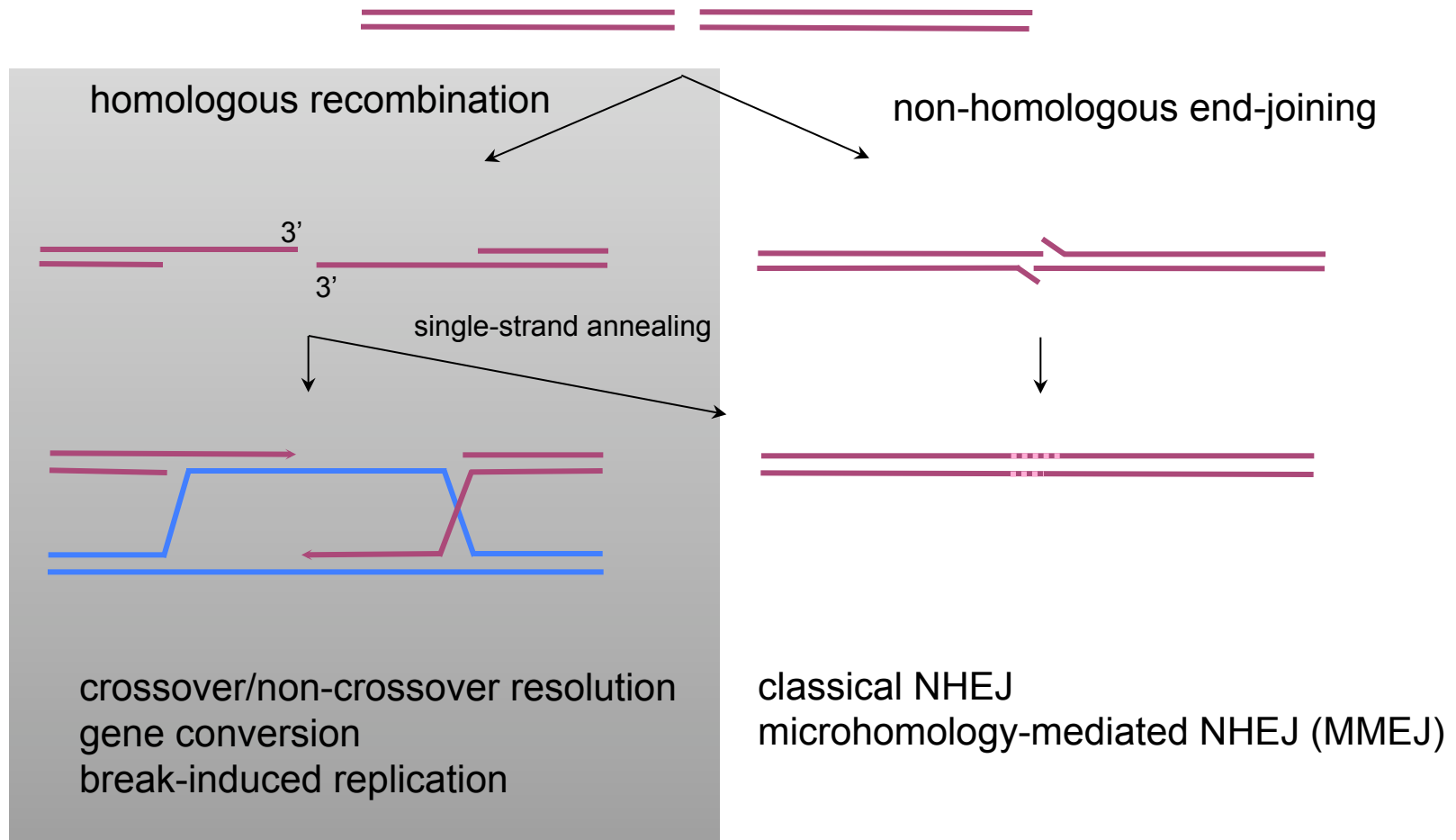
MD Anderson Science Park/ NIH videoconference

12/08

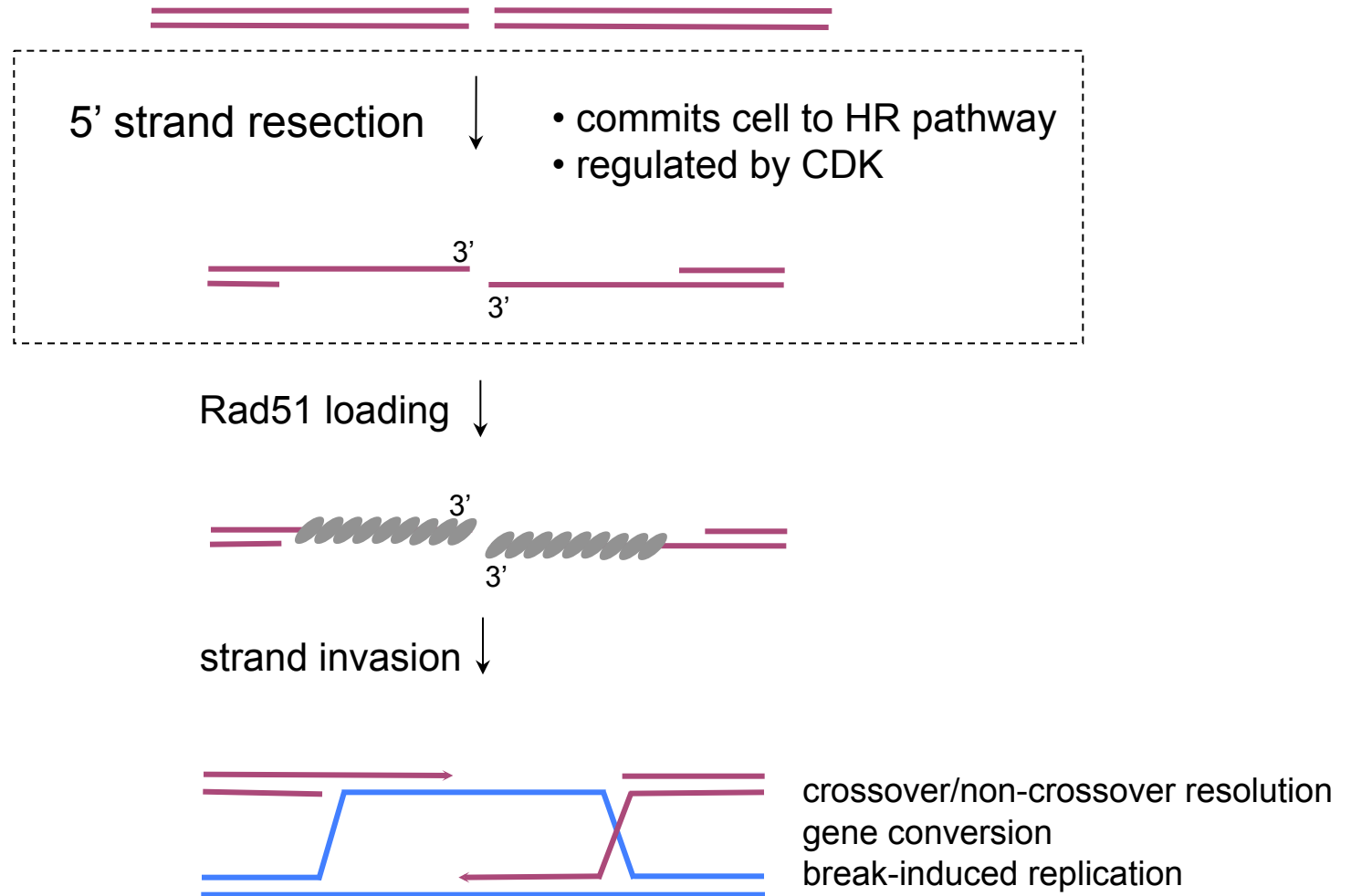
The DNA damage response in eukaryotic cells:



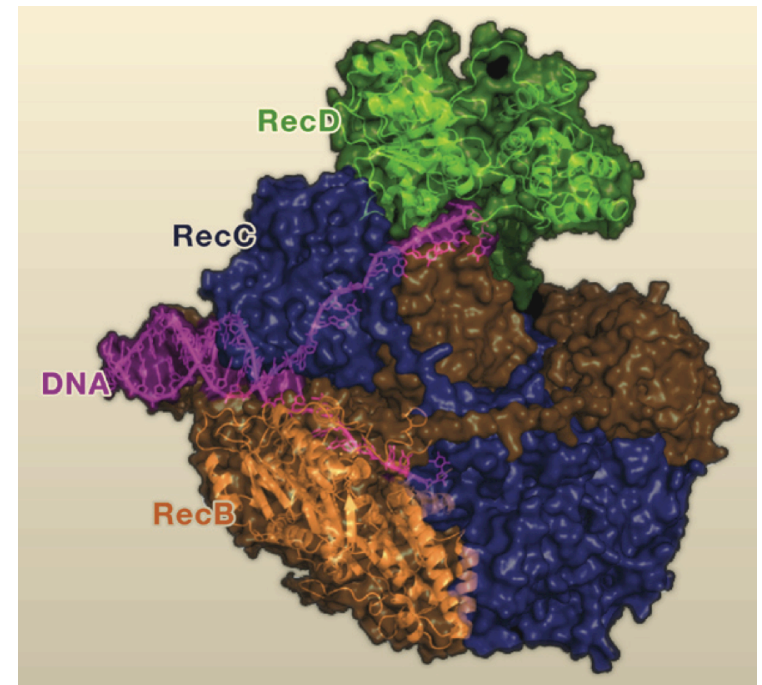
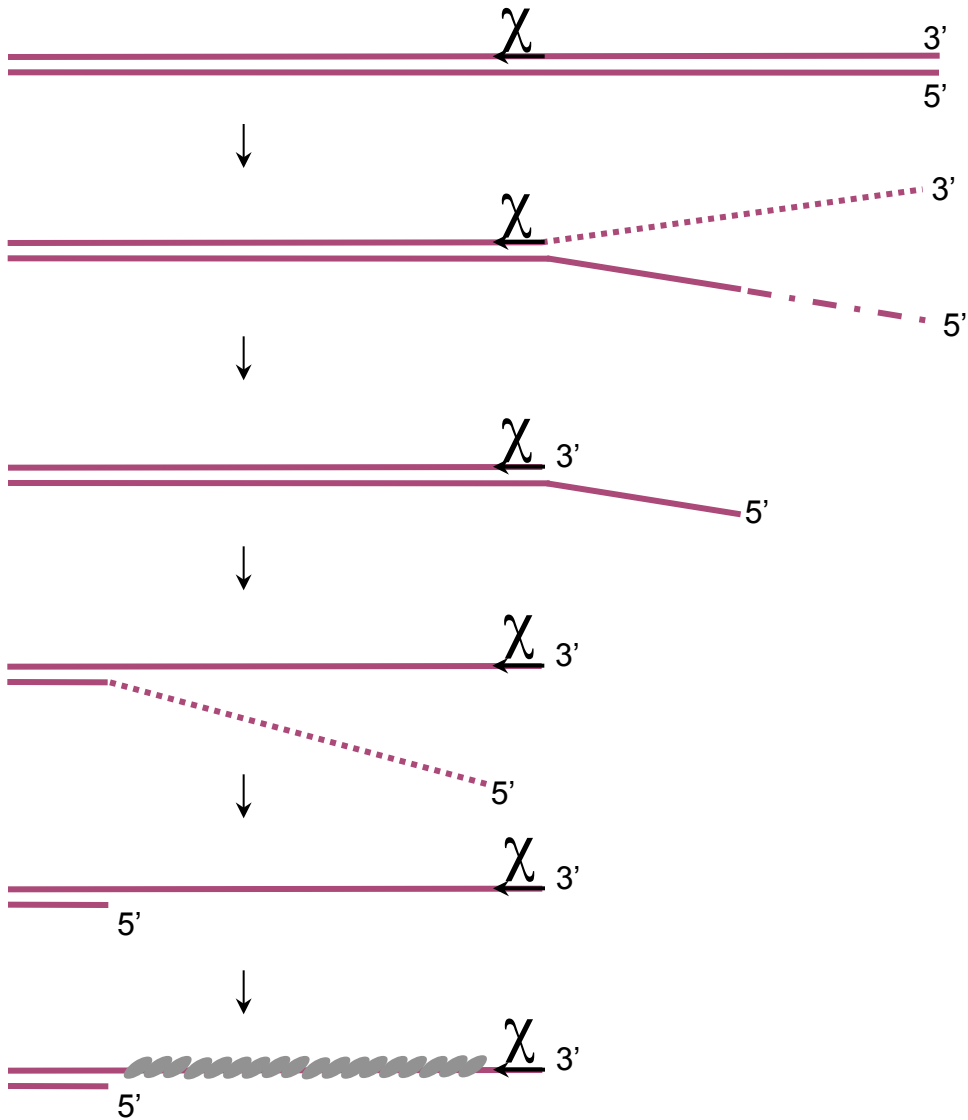
Pathways of Double-Strand Break Repair:



Processing of DNA ends for homologous recombination in eukaryotes:



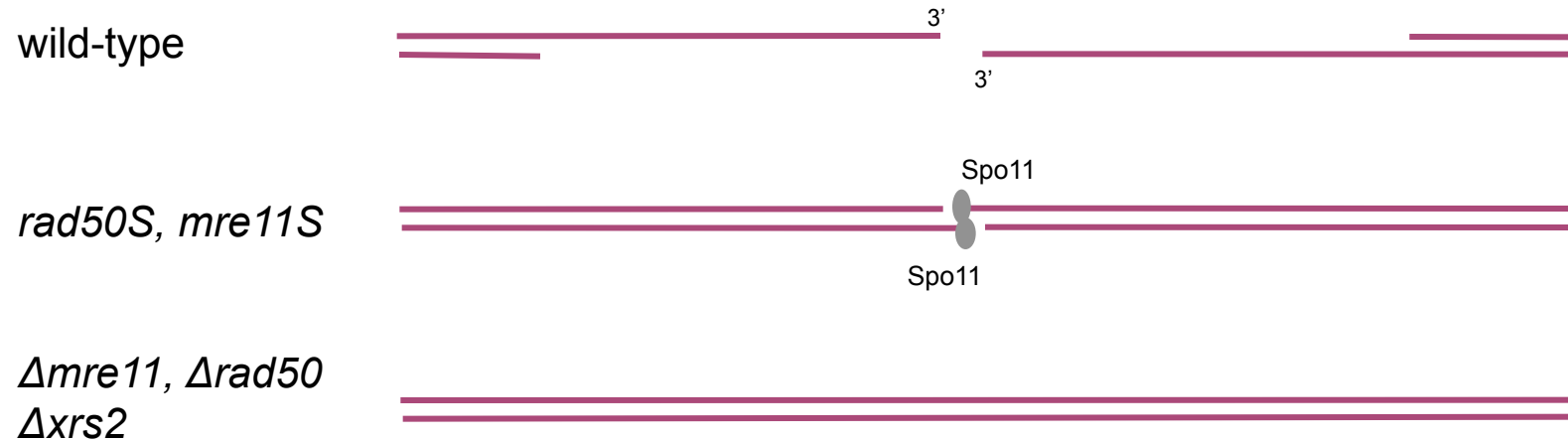
RecBCD-mediated processing of DNA breaks in bacteria:



Singleton, M.R., Dillingham, M.S., Gaudier M., Kowalczykowski, S.C., and Wigley, D.B. (2004) Nature 432: 187-193.

but orthologs of RecBCD not
apparent in archaea or eukaryotes

Phenotypes of *rad50* and *mre11* mutants during meiosis:

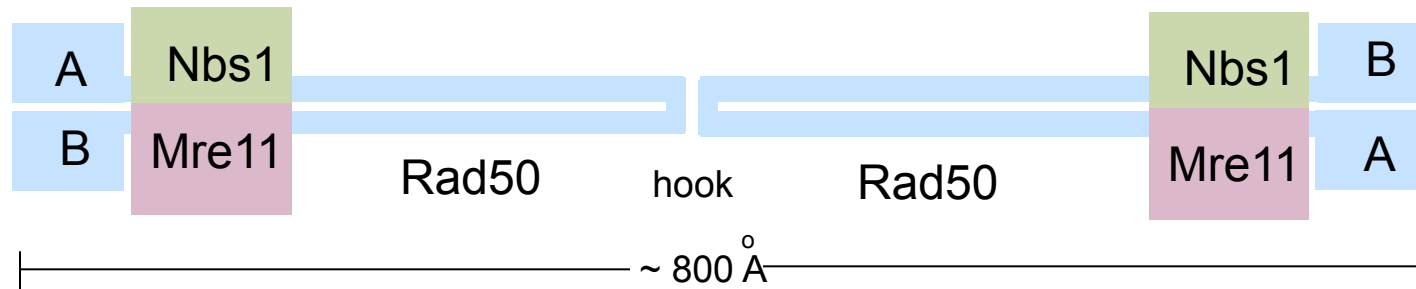


Mre11 and Rad50 inferred to play a role in resection based on resection defects during meiosis

Alani, E., Padmore, R., and Kleckner, N. (1990). Analysis of wild-type and *rad50* mutants of yeast suggests an intimate relationship between meiotic chromosome synapsis and recombination. *Cell* 61, 419-436.

Nairz, K., and Klein, F. (1997). *mre11S*--a yeast mutation that blocks double-strand-break processing and permits nonhomologous synapsis in meiosis. *Genes & Dev.* 11, 2272-2290.

Mre11/Rad50/Nbs1(Xrs2)



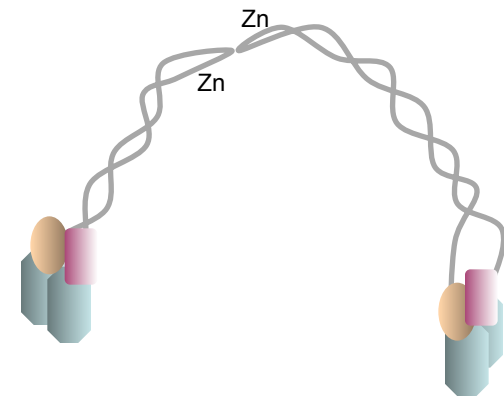
Mre11:

3' to 5' exonuclease and endonuclease on hairpin loops and ss/ds transitions

Rad50: ATPase in the ABC transporter family; similar to the Structural Maintenance of Chromosomes (SMC) family of chromosome condensation and chromatid cohesion proteins

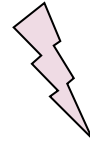
Nbs1 (mammals) or **Xrs2** (yeast): regulatory component, only found in eukaryotes, controls both Mre11 and Rad50 enzymatic activities

zinc-mediated hook associations mediate intermolecular connections between Rad50 molecules:

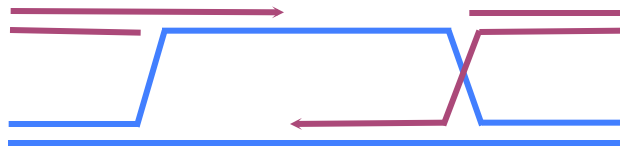


Functions of the Mre11/Rad50/Xrs2 complex in *S. cerevisiae*:

→ required for survival of DNA double-strand breaks



→ required for S-phase checkpoint response



homologous recombination



non-homologous end joining (NHEJ)

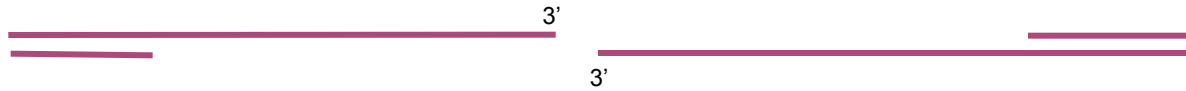


→ telomere maintenance



→ meiotic recombination

The polarity paradox:



DNA ends are resected from 5' to 3' but...

- The direction of Mre11 exonuclease activity in vitro is 3' to 5'
- resection of DNA ends in vegetatively growing cells is not dependent on Mre11 nuclease activity (even though meiotic DSB resection is Mre11 nuclease-dependent).

Yet...

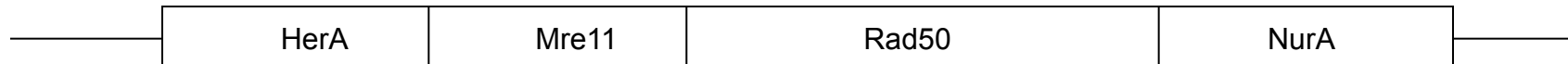
- overexpression of Exo1 (5' to 3' exonuclease) can suppress DNA repair defects seen in MRX-deficient strains

Paull, T.T., and Gellert, M. (1998). Mol. Cell 1, 969-979.

Moreau, S., Ferguson, J.R., and Symington, L.S. (1999). Mol. Cell. Biol. 19, 556-566.

Moreau, S., Morgan, E.A., and Symington, L.S. (2001). Genetics 159, 1423-1433.

The Mre11 and Rad50 genes cluster with a helicase (HerA) and a nuclease (NurA) in thermophilic archaea:



? Do Mre11, Rad50, HerA, and NurA form a multisubunit enzyme for DNA end processing ?

Pyrococcus furiosus: thermophilic archaeon, grows at high temperatures (75 - 100°C)

- HerA from *Sulfolobus* and *Pyrococcus* species exhibits both 5' and 3' helicase activities in vitro
- NurA resects linear dsDNA from 5' to 3' and also exhibits endonuclease activity on ssDNA

F. Constantinesco, P. Forterre, and C. Elie (2002) EMBO Rep. 3: 537-542.

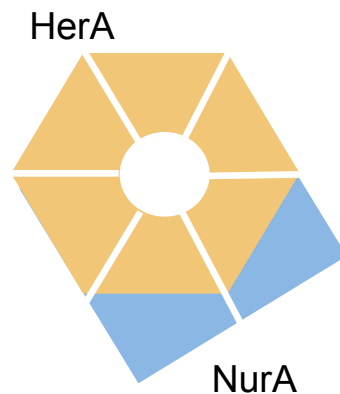
F. Constantinesco, P. Forterre, E.V. Koonin, L. Aravind, and C. Elie (2004) NAR 32: 1439-1447.

A. Manzan, G. Pfeiffer, M.L. Hefferin, C.E. Lang, J.P. Carney, and K.P. Hopfner (2004) EMBO Rep. 5: 54-59.

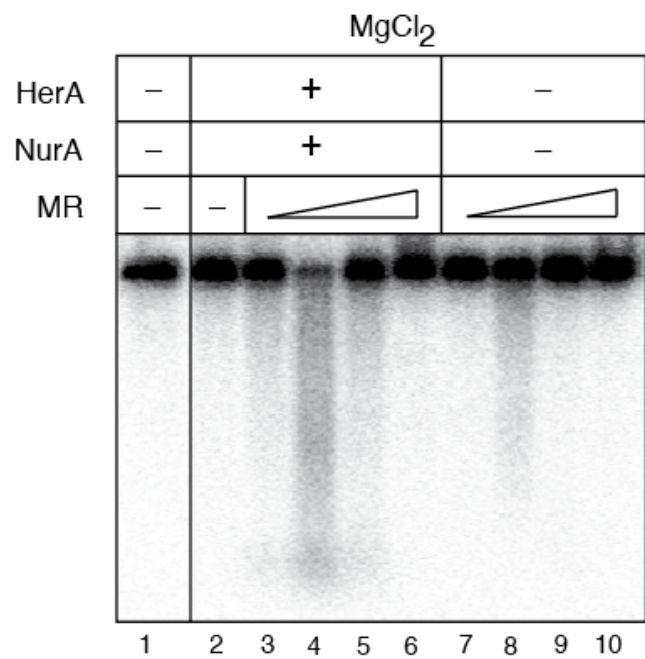
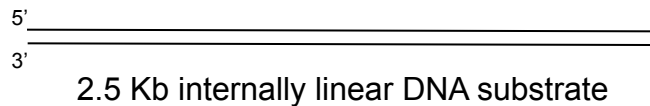
S. Zhang, T. Wei, G. Hou, C. Zhang, P. Liang, J. Ni, D. Sheng, and Y. Shen (2008) DNA Repair 7: 380-391.

Recombinant pfHerA (helicase) and pfNurA (nuclease) are functionally interdependent:

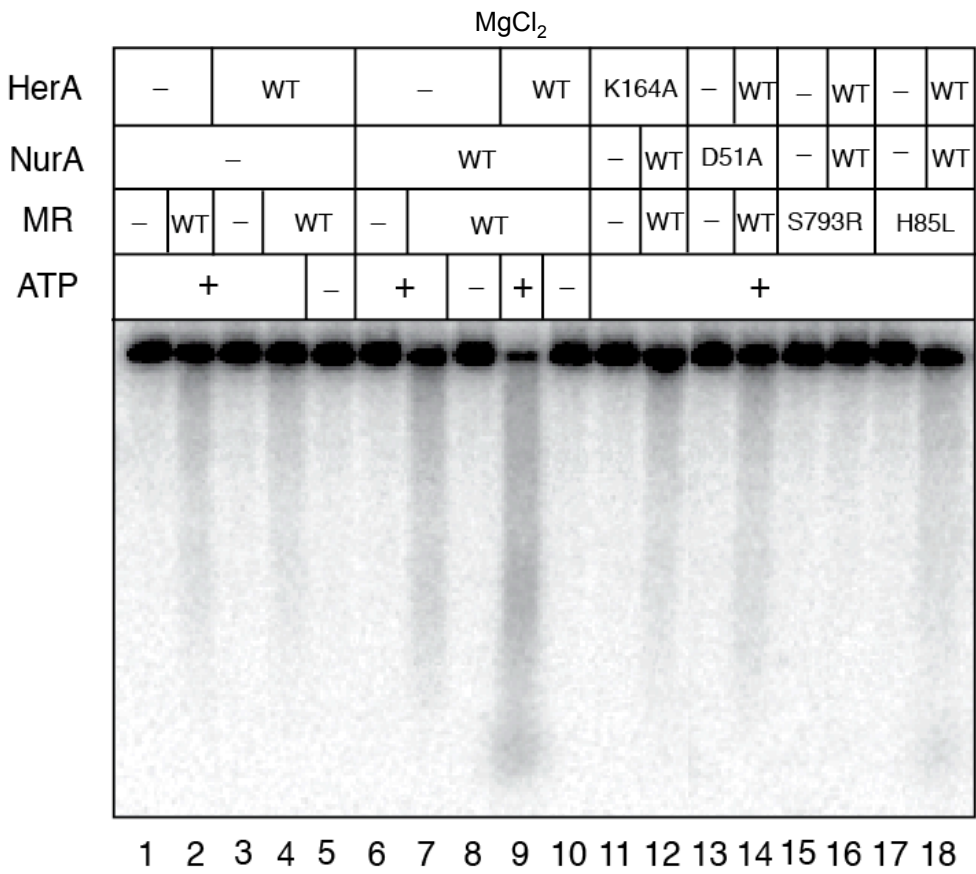
- pfHerA and pfNurA physically interact in the absence of DNA or ATP
- no detectable interactions between pfHerA/NurA and pfMre11/Rad50
- pfNurA is a Mn-dependent 5' – 3' exonuclease but shows activity in Mg in the presence of pfHerA
- pfHerA helicase activity is stimulated ~3 to 5-fold by pfNurA



Recombinant pfMre11/Rad50 stimulates resection of linear DNA ends by pfHerA/NurA by ~20-fold:

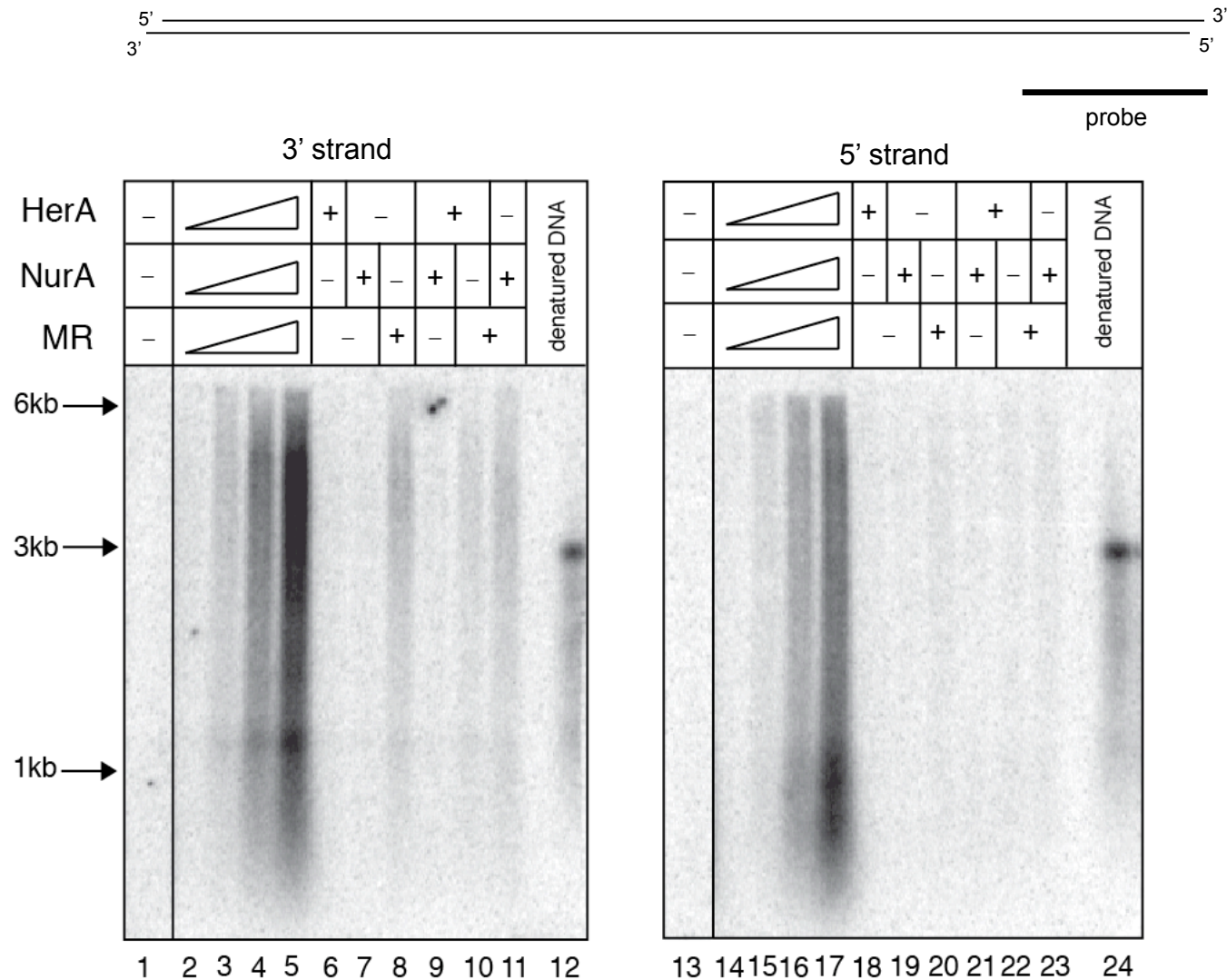


20 nM NurA (monomer)
2.7 nM HerA (hexamer)
0.3, **3.3**, 33, 330 nM Mre11/Rad50 (M2R2)
1 hr, 65°C



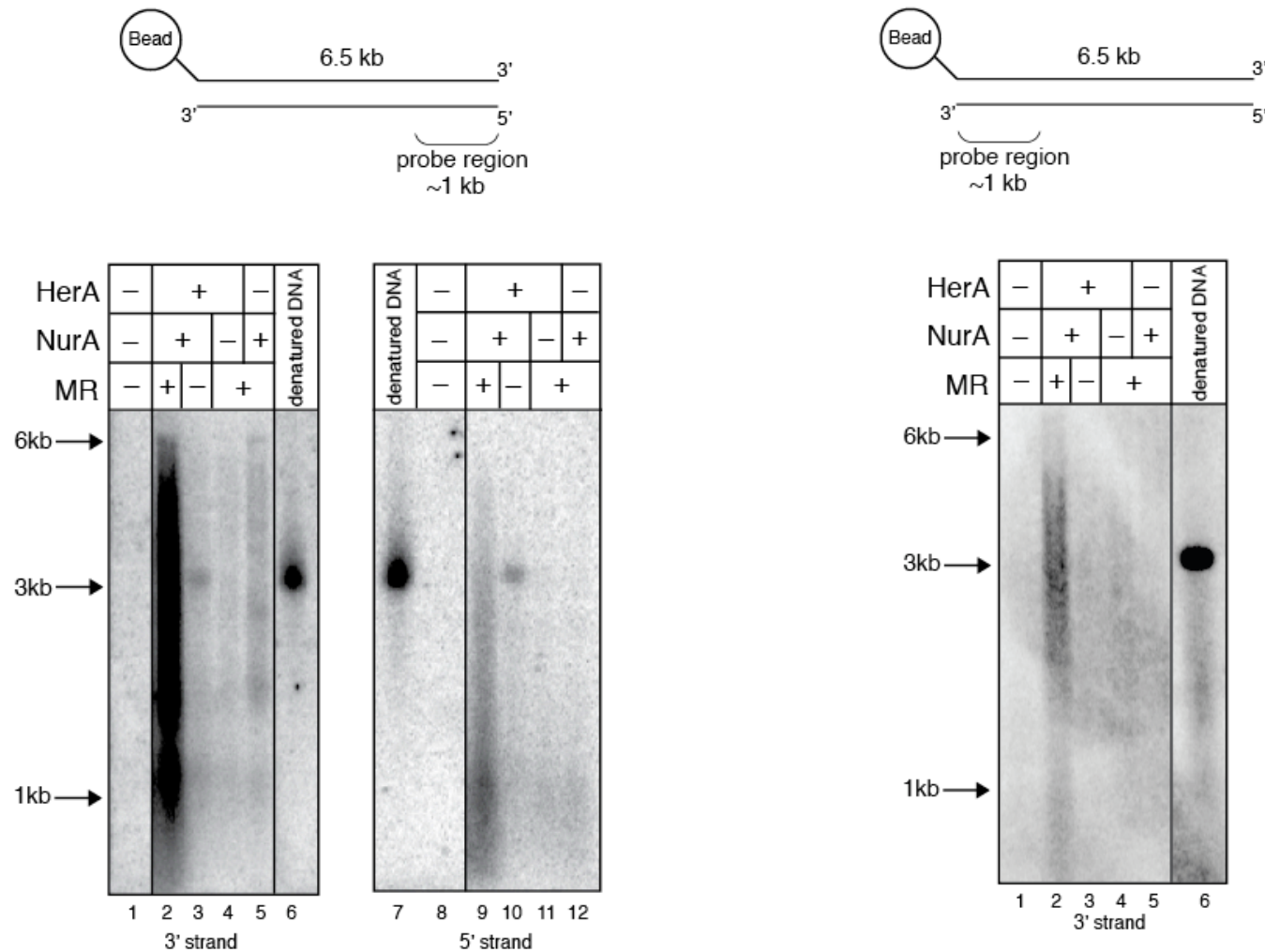
20 nM NurA (monomer)
2.7 nM HerA (hexamer)
3.3 nM Mre11/Rad50 (M2R2)
1 hr, 65°C

Strand-specific probes show resection of both strands, but more pronounced resection of the 5' strand:



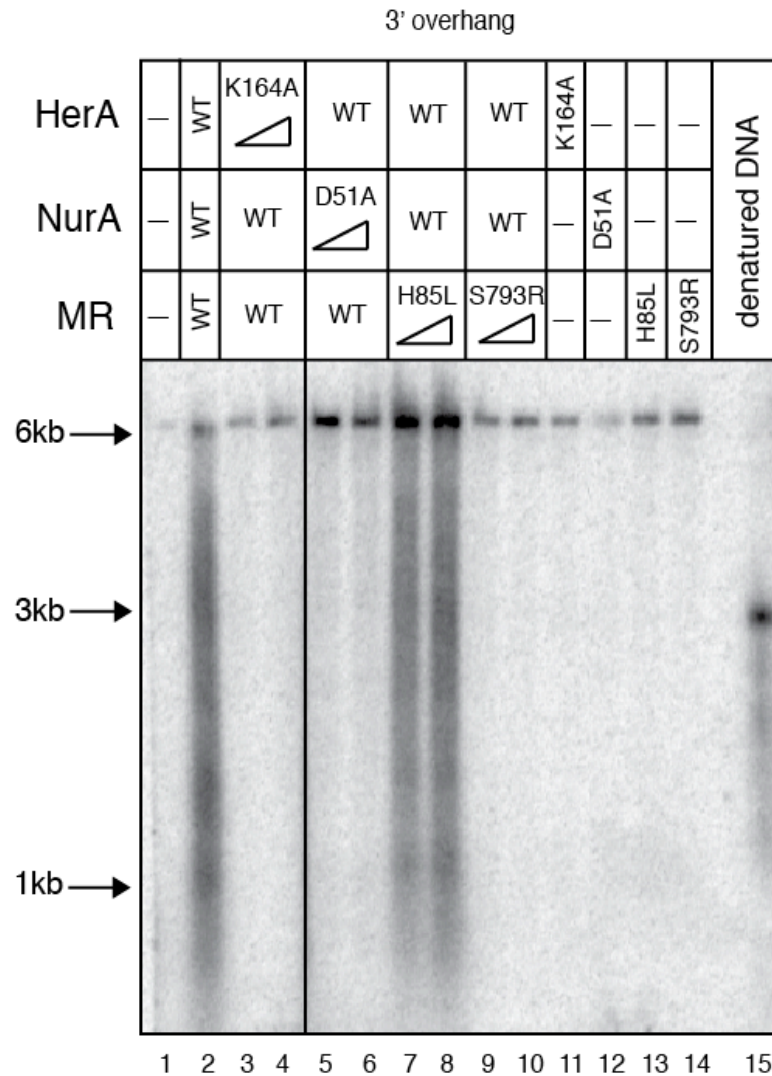
5, 10, 20, 40 nM NurA (monomer); 0.7, 1.4, 2.7, 5.4 nM HerA (hexamer); 0.8, 1.6, 3.3, 6.6 nM Mre11/Rad50 (M2R2), 5 mM MgCl₂, 1 mM ATP, 15 min, 65°C

The direction of pfMRHN-catalyzed resection is 5' to 3':



40 nM NurA (monomer); 5.4 nM HerA (hexamer); 6.6 nM Mre11/Rad50 (M2R2)
5 mM MgCl₂, 1 mM ATP, 65°C

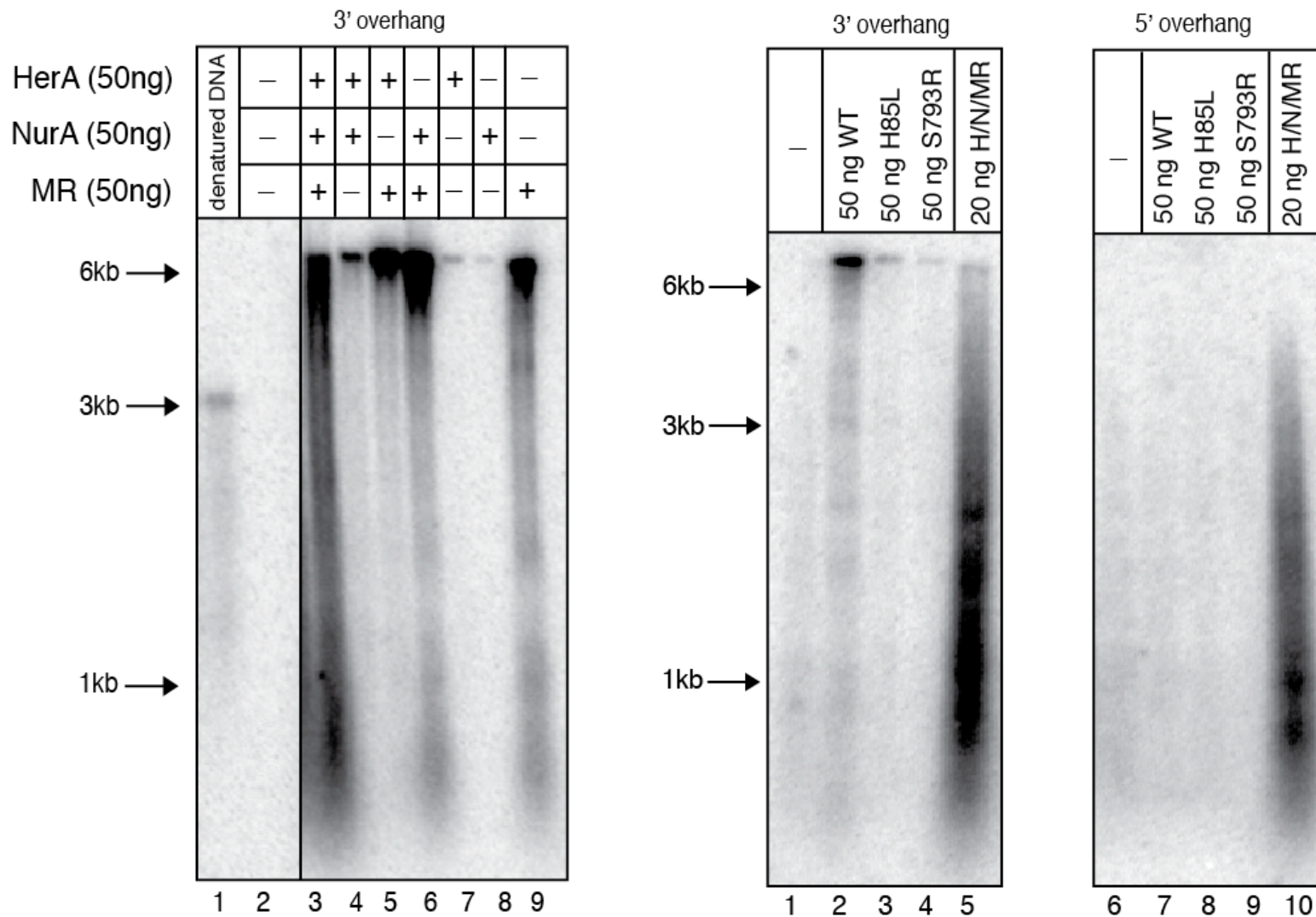
Cooperative DSB resection requires catalytic activities of pfRad50, pfHerA, and pfNurA, but not pfMre11:



20, 40 nM NurA (monomer); 2.7, 5.4 nM HerA (hexamer); 3.3, 6.6 nM Mre11/Rad50 (M2R2)
5 mM MgCl₂, 1 mM ATP, 15 min, 65°C

Ben Hopkins

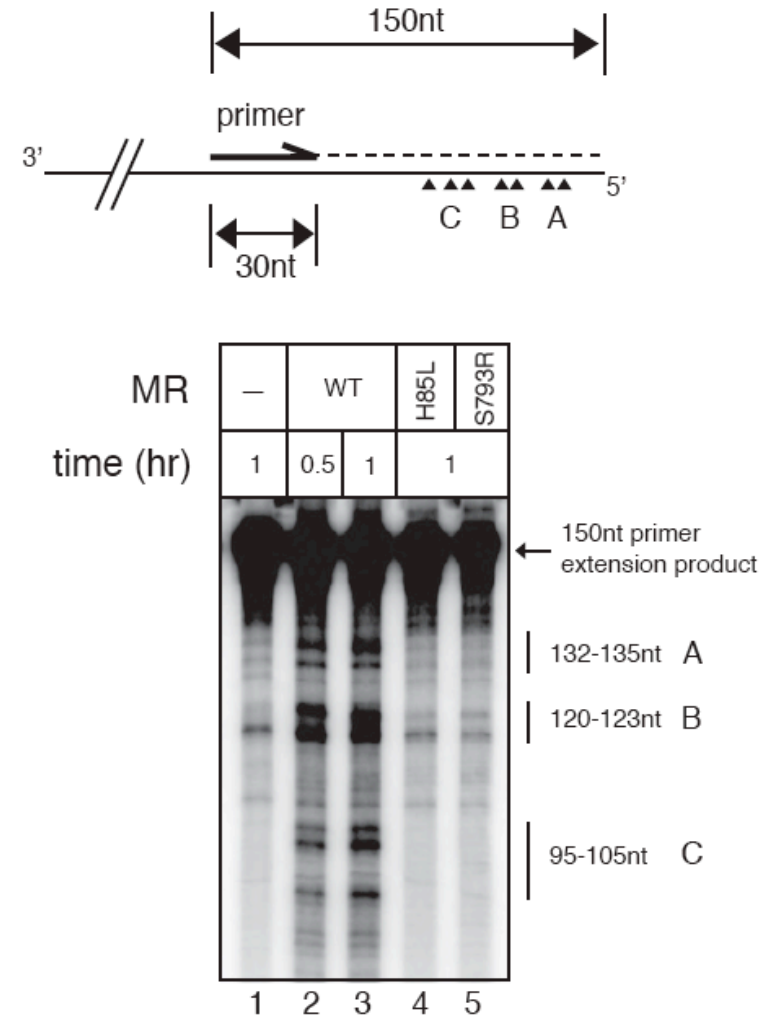
pfMre11/Rad50 catalyzes short-range resection of the 5' strand of a DSB, dependent on the nuclease activity of pfMre11:



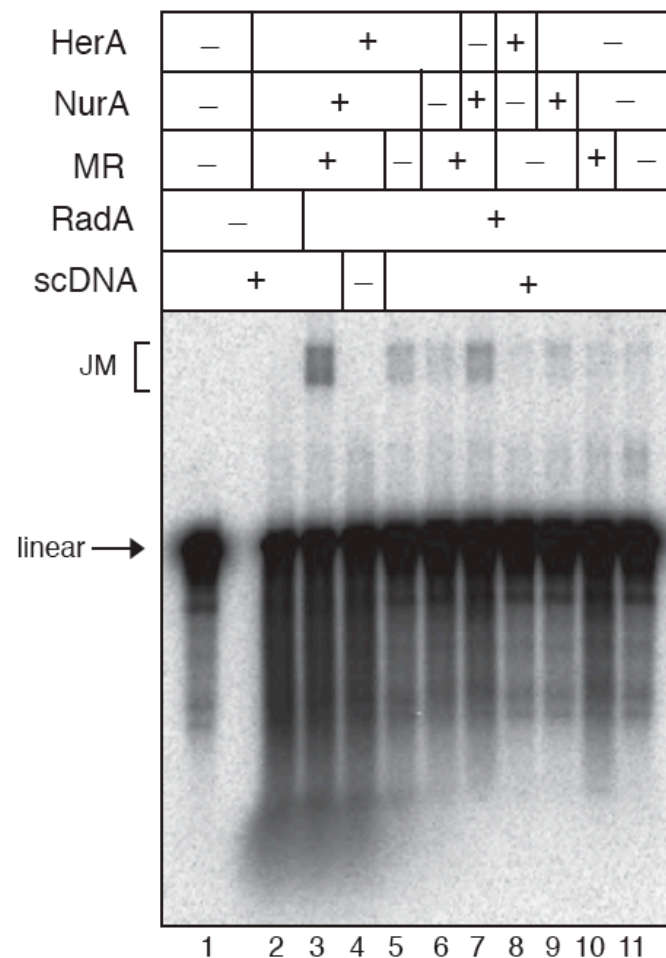
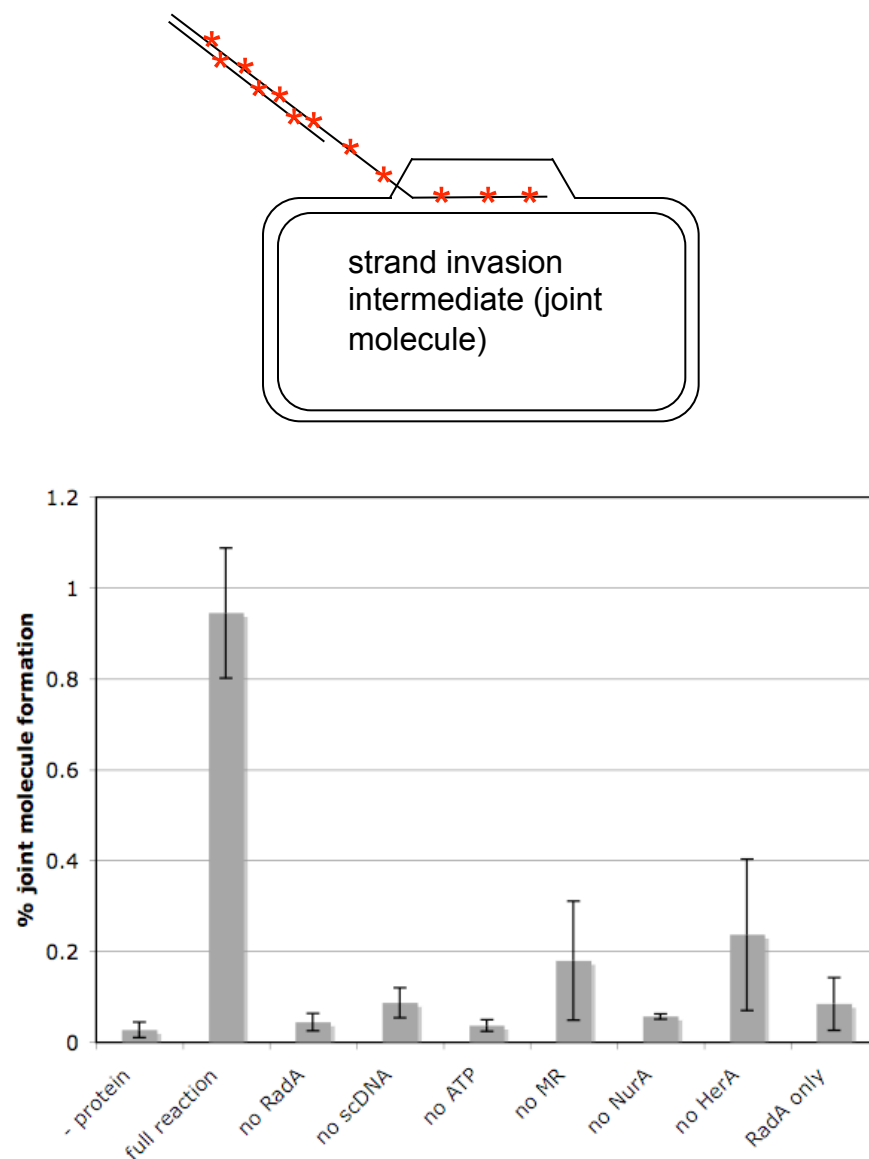
50 ng = 100 nM NurA (monomer); 13.5 nM HerA (hexamer); 16.5 nM Mre11/Rad50 (M2R2)
5 mM MgCl₂, 1 mM ATP, 15 min, 65°C

pfMre11/Rad50 does exhibit
nuclease activity in MgCl_2 at
physiological temperature:

endonucleolytic cleavage
events on the 5' strand

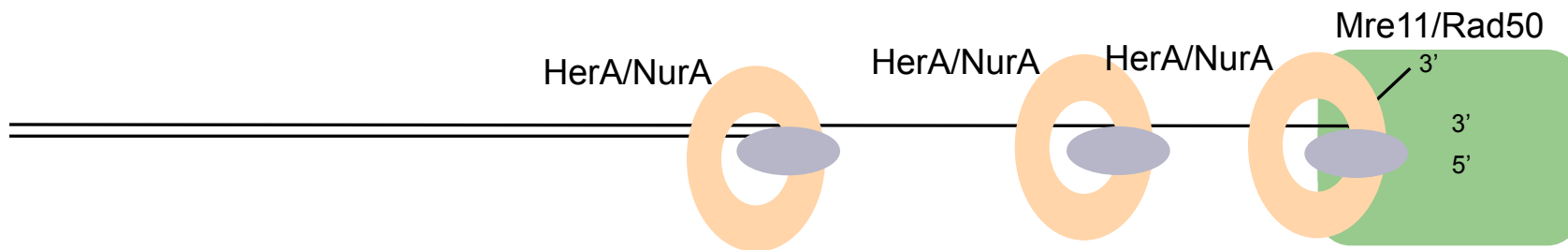


pfMRHN function cooperatively with pfRadA in strand invasion:



200 nM NurA (monomer); 27 nM HerA (hexamer); 33 nM Mre11/Rad50 (M2R2); 50 nM RadA; 10 mM MgCl₂; 2 mM ATP; 0.2 nM linear DNA; 2 nM scDNA; 30 min, 55°C

Working model for DSB processing by pfMre11/Rad50/HerA/NurA:



Double-strand break processing in eukaryotes:

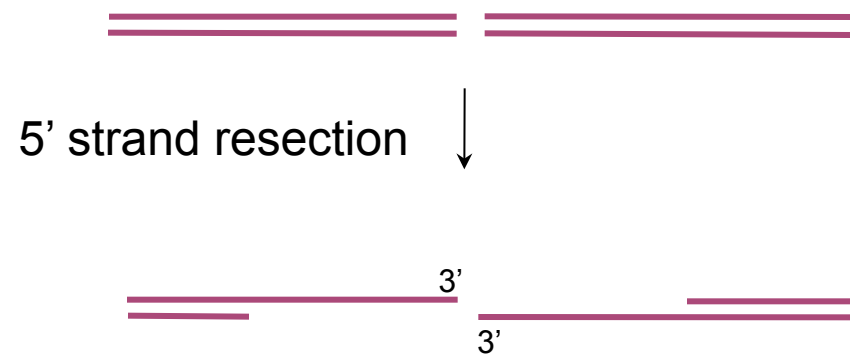
Factors implicated in DNA end processing in *S. cerevisiae*:

- Mre11/Rad50/Xrs2 (MRX)

- Sae2

- Exo1

- Sgs1(Rmi1/Top3)/Dna2



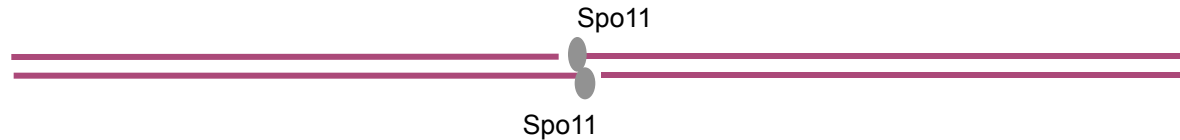
Removal of any single complex results in a delay of resection in vivo;
resection completely blocked by removal of MRX/Sae2 + Exo1 + Sgs1/Dna2

Mimitou, E.P. and Symington, L.S. (2008) Nature 455: 770-774.

Zhu and Ira, G. (2008) Cell 134:981-994

Gravel, S., Chapman, J.R., Magill, C., and Jackson, S. P. (2008) Genes & Dev. 22:2767-2772.

Sae2 and the Mre11/Rad50/Xrs2 (MRX) complex in *S. cerevisiae*:



- Sae2 is required for the processing of double-strand breaks made by Spo11 during prophase of meiosis I; phenotype similar to that of Rad50S (covalent, unprocessed Spo11-DNA conjugates)

McKee, A. H., and Kleckner, N. (1997) *Genetics* 146, 797-816.

Prinz, S., Amon, A., and Klein, F. (1997) *Genetics* 146, 781-795.

- Sae2 also is important for chromosomal DNA repair in vegetative cells (assay for intrachromosomal homologous recombination)

Rattray, A. J., McGill, C. B., Shafer, B. K., and Strathern, J. N. (2001). *Genetics* 158, 109-122.

- Sae2 (and MRX) are essential for the processing of hairpin-capped double-strand breaks

Lobachev, K. S., Gordenin, D. A., and Resnick, M. A. (2002). *Cell* 108, 183-193.

Rattray, A. J., Shafer, B. K., Neelam, B., and Strathern, J. N. (2005). *Genes Dev* 19, 1390-1399.

Sae2 phosphorylation and effects on DSB processing:

- Sae2 is phosphorylated on several SQ/TQ sites during S/G₂ and after DNA damage



Baroni, E., Viscardi, V., Cartagena-Lirola, H., Lucchini, G., and Longhese, M. P. (2004). Mol Cell Biol 24, 4151-4165.

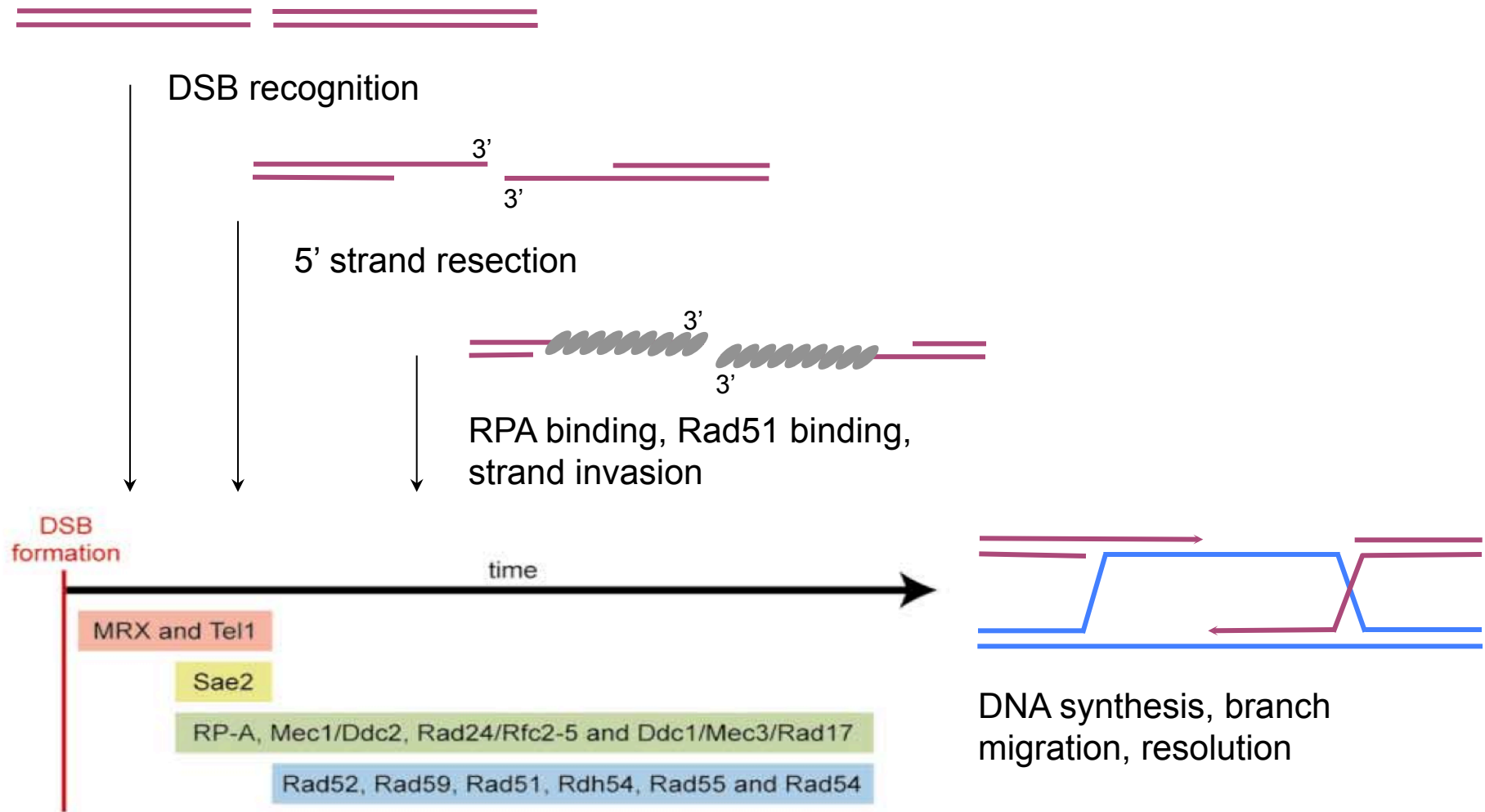
- In the absence of Sae2 (or Δ MRX or MRX(Rad50S)), processing of DSBs into 3' single-strands is delayed and the efficiency of single-strand annealing is significantly reduced

Clerici, M., Mantiero, D., Lucchini, G., and Longhese, M. P. (2005). J Biol Chem 280, 38631-38638.

- Sae2 is phosphorylated in S/G₂ by CDK on S267; mutation of this serine to the phosphomimic glutamate can drive resection in G₁ phase

Huertas, P., F. Cortes-Ledesma, A.A. Sartori, A. Aguilera, and S.P. Jackson. 2008. CDK targets Sae2 to control DNA-end resection and homologous recombination. Nature 455: 689-692.

Microscopy and chromatin immunoprecipitation assays show that MRX and Sae2 localize to DNA breaks first, then dissociate with Rad51 loading:



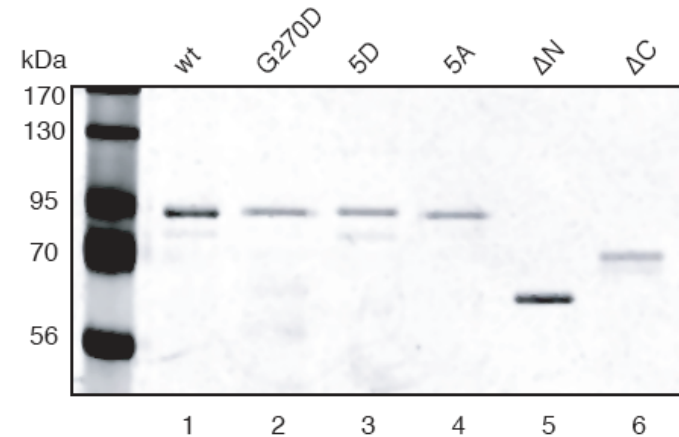
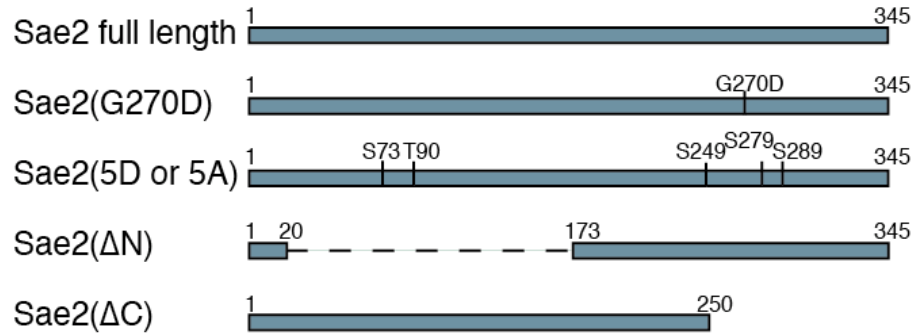
Lisby M, Barlow JH, Burgess RC, Rothstein R (2004) Choreography of the DNA damage response: spatiotemporal relationships among checkpoint and repair proteins. Cell 118(6): 699-713

Sae2:

S. cerevisiae SAE2	MVT--GEENV	YLK-----	---SSLSIL	KELSLDE--	-LLNVQYDVT	-----TL	IAKRVQALQN	RNKCYLEEPN	SKLAEILCH-	64
A. gossypii SAE2	MLVQEGPPST	QQY-----	---EIKDWL	RGLSWEH--	-LVSLQYDIA	-----DE	LARRVREMKL	ASG-LSKDKE	DHTEELIST-	65
C. glabrata SAE2	M-----PND	-----	---EIKTV	TAMNVTQ--	-LLDLQ---	-----DF	ITKTLRERLI	NPSNDLKSTE	DQPKVELLPN	54
K. Lactis SAE2	M-----SQE	SEE-----	---SLEAWL	HRLEWSQ--	-LLSLQKQLV	-----SE	MDRRY-----	-----	---VEII---	40
Y. lipolytica SAE2	MEKAKKSVEI	LET-----	---ELAVLK	EALDSVQNSP	TASSVKQEF	QTPTNLPRSD	LQEQYDKLAL	SHAKLIKLRK	GDIKSVNLWK	79
D. hansenii SAE2	MKELPETIEV	YHELVGRQIQ	DILQENRELK	MKLEKQENQL	RSIRIQYKSD	IQALRDDASD	LEAVNNEFKE	IIRNIGVPPK	NKTQKVRVFQ	90
Consensus	M---G-PXV	YEE-----	---EXXXL	XALXWXQ---	-LLSLQYDXX	-----SX	LAXRXRELKL	XXXNLLKXPX	DKTKEVXLX-	
S. cerevisiae SAE2	-EK-----	-NA-----P	QSSQTSAGP	-----GEQDS	ED-----	-----FILTQF	DE-DIKK-ES	AEVHYRNENK	HTVQL--PLV	118
A. gossypii SAE2	-QT-----	-SATEAVQP	QTGYLHMGAP	STFPEGDGDS	QPLIPGTLEL	RNKHFVLSS-	-S-PLKK-EL	PESQ-NSQNS	PRRNL--RLL	138
C. glabrata SAE2	EIQE-----	-EGKVDGKP	KNGNLVTVLQ	VK-REDSQDS	DD-----	-----FILTQF	DSQDVGS-AK	KQSQFEKSS-	-----	111
K. Lactis SAE2	-----	-----QP	QQQNIQDDL	EYMKDGLSSY	DDLPS-----	-----TQF	DPIHVKKNAT	VKSTIEQEHA	EPLAR--ERN	98
Y. lipolytica SAE2	EALQ-----	-DHKGRLKE	SQGQVLELK-	---KENQILK	DEIQELKKIK	QEQTVAIQT	SQTCPSDEI	TTEQIRAEAG	EPVEITNELL	157
D. hansenii SAE2	DRRERLPMTP	LTNKKRKLSE	SNESISEDES	PLSQTVPKST	QPISDVKYAT	NHPLQLPTQY	SSDSTASIER	PVYNKDNNGS	PRLMYQGGK-	178
Consensus	--QE-----	--NAK--LXP	QXGXXXEDLP	---KEGXQDS	DDX-----	----FXLTQF	DS-DVKX-EX	PESQIXNENS	XXXXL--ELL	
S. cerevisiae SAE2	TMPPNRHKR-	-----	---KISEFSS	PLNGLNNLSD	L-----	-EDCSDTV-I	HEK-DND---	---KENKTR	KLLGIELEN-	174
A. gossypii SAE2	-LGPR LAPK-	-----	---QSSPTKS	PRRSPTKEVS	T-----	-PRAKQTQEA	HEPIDED---	---EAEQIS	DSEG-DL-S-	193
C. glabrata SAE2	-----IKPE-	-----	---FSSPLKF	SQVSNDKAD	N-----	-PLPKEVCHA	NGGDHLS---	---IEKTIP	FKRRDLLENI	165
K. Lactis SAE2	QQLQRDLLEL	-----	---MSSPLKE	NEIILDSQAS	D-----	-ILKENDINI	QSHQSV---	---IAKSKR	GRSPINATTM	157
Y. lipolytica SAE2	RSSPPFGKKG	LLIKDSIDL	AVEHSSPSVS	REIDPDLEND	TRRHQGVVFK	QPKPTNLMQW	LKVKEEN---	---IGQDIT	KSNKRDVEVV	240
D. hansenii SAE2	---PFDRD	DFTDSQDFML	PTQYSSQDNE	NEIDLKSKLD	NASQ--IVVK	EENKENFDEI	EDSQDEFPLD	SFELIKKPI	KVKREPLENI	261
Consensus	---PRXXX-	-----	---XSSPLKS	XEIXLDXXAD	X-----	-PLXXNTXEI	HESXDED---	---IXKXRR	KSXXIDLNI	
S. cerevisiae SAE2	---PESTSP	NLYK-----	-----	---NVK----	DNFLDFDNTN	PLTKRAWILE	DFRPNEDIAP	VKR--G-R-	---RKLERF	228
A. gossypii SAE2	---WDSKLP	DVHE-----	-----	---GQE----	KRAKIDFNTN	PIAKRPWIYE	DFQANHEVLE	-EL--S-K-	---KRLKDH	246
C. glabrata SAE2	KEYDWKWSHH	NDKV-----	-----	---QNN----	KQSILDFNKN	PFSKRPWILE	DFCPNSNAIA	KKK--H-E-	---IDFEKF	223
K. Lactis SAE2	PQANRRNEKE	NIKR-----	-----	---G-----	-KISVDFSIN	PITKKPWIE	DFKINELVSS	KNR--G-RG	CKKSNKVARF	217
Y. lipolytica SAE2	DLDSQGSPE	KTKK-----	-----	---SRKSCPA	QYQLTDFVIN	PAFNGDL---	DFAYAETVRG	SRR--QCEH	GGECRQCDEF	305
D. hansenii SAE2	TSKFNSQSQS	QLHPKVPSHY	TKLQRRAYLK	EYYESKFHKS	PGFKIDLNSN	PINEMEWIIN	DFKPNPNYVK	SNQVKGNAIS	KNDQNNVDRF	351
Consensus	---WXSSKX	NLKK-----	-----	---GXX----	KXFXIDFNXN	PITKRPWIE	DFKPNENVXX	XXR--G-X-	---XXXXRF	
S. cerevisiae SAE2	YAQVGKPEDS	KHR-----	---SLSVIE	SQNS--DYE	FA--FDNLR	NR--SKSPP	GFGRLDFPST	QEGNEDKKKS	QEIRRKTKY	299
A. gossypii SAE2	RRNVMDGLAG	LPN-----	---KLGGEAN	YDSSF--DES	FPM--YDNL	HR--SKSPP	GYGRLDFTT	QEIQDDKRKA	QDMIYQRTKH	319
C. glabrata SAE2	QKKVSNFIEN	KTN-----	---NAKESDI	ECAKY--EGR	LRNIHFDNMR	NR--SPSPP	GYGRLDFTT	QERADDKSKA	QSIIRDKTL	298
K. Lactis SAE2	HAQAGSPLKS	KQNVVLNSTG	LLETVDTSV	SDRSKVPDLQ	FPDDSFNLR	VR--SKSPP	GYGRLDFTT	QERLDDKEES	RKLLYQKTKT	304
Y. lipolytica SAE2	YKMAQPGIYS	AA-----	---PQWSATED	KERGRKMDIE	ETINASSRHR	NRWKRAPSP	GFWRSDFTT	QEIVEEKCLA	EENRRKEIEI	385
D. hansenii SAE2	YQLAGP---	-----	---LPKVPQLTW	NNEVIESDND	SIGLSSESQVL	DKY--PSPP	GFMVSEFPDT	QEQHMRNRII	DERQEDRIKR	423
Consensus	YXQXGPXXXS	KXN-----	---KXSETXX	SDRSX--DXE	FPM--YDNL	NR--SKSPP	GFGRLDFPST	QEXXDDKXKA	QEIRRKTKY	
S. cerevisiae SAE2	RFLMASNNKI	PPYEREYVFK	REQLNQIVDD	GCFWSDKLL	QIYARC					345
A. gossypii SAE2	RFKMAVQRKI	PIFEREYFFK	NPQLNTWVDN	GEISWSKEEL	QIFKRT					365
C. glabrata SAE2	RFLSATNNRV	PPMKREFLEK	KRELNDVVD	GNFDWTEESL	EIFSR					343
K. Lactis SAE2	RFLSATNNLV	PISEREFYFR	NSKLNDIVDD	GNFTWNEENEL	KIFTR					349
Y. lipolytica SAE2	RYKSAVSG--	---GKWMFR	---	GK-----DQ	---	---	---	---	---	407
D. hansenii SAE2	RVKQCIRSS-	RNKNGEFIFQ	VDILNKFAQQ	NRFNYD---	---	---	---	---	---	459
Consensus	RFXAXXNNKX	PXXEREFXFK	NXQLNDIVDD	GNFXWSEEL	QIFXR-					

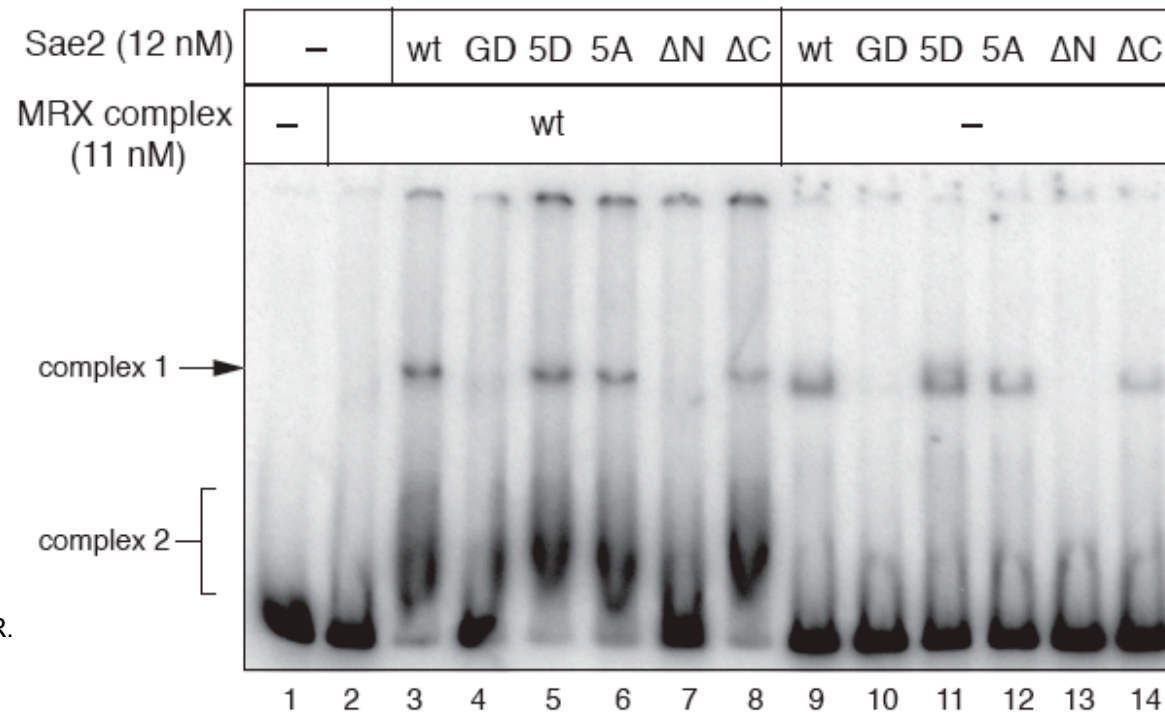
Sae2 phosphorylation: Baroni, E., Viscardi, V., Cartagena-Lirola, H., Lucchini, G., and Longhese, M. P. (2004). Mol Cell Biol 24, 4151-4165.

Recombinant Sae2:



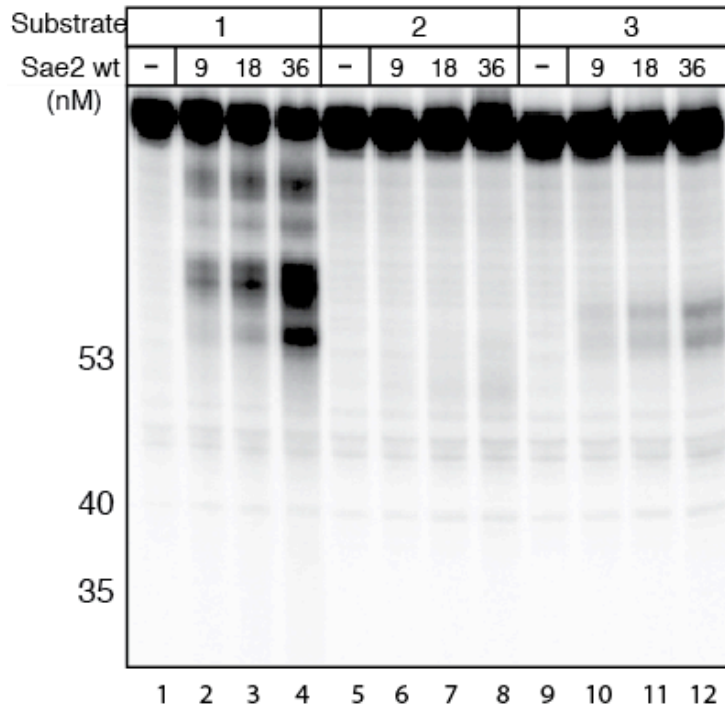
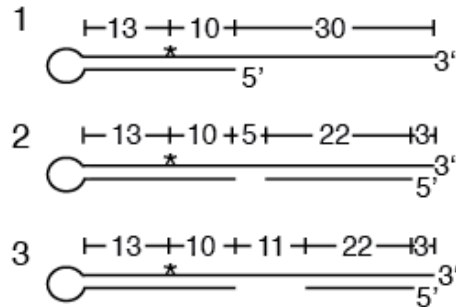
- dimeric and monomeric forms

- binds linear DNA; forms complexes in response to MRX

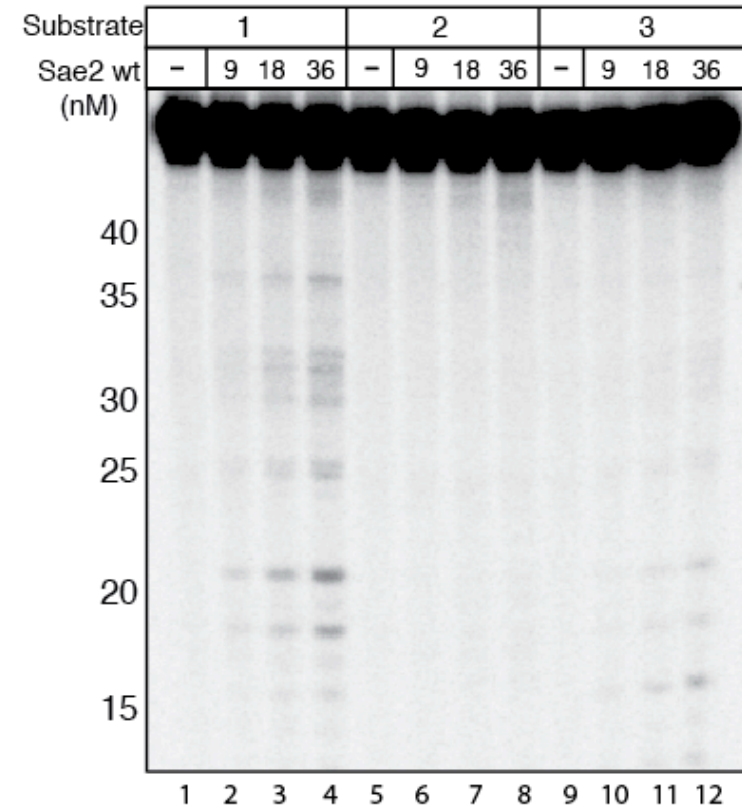
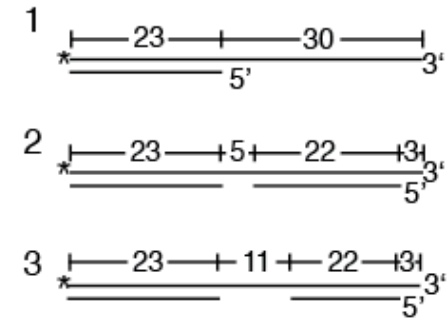


Lengsfeld, B.M., A.J. Rattray, V. Bhaskara, R. Ghirlando, and T.T. Paull, (2007) Mol Cell, 28:638-51.

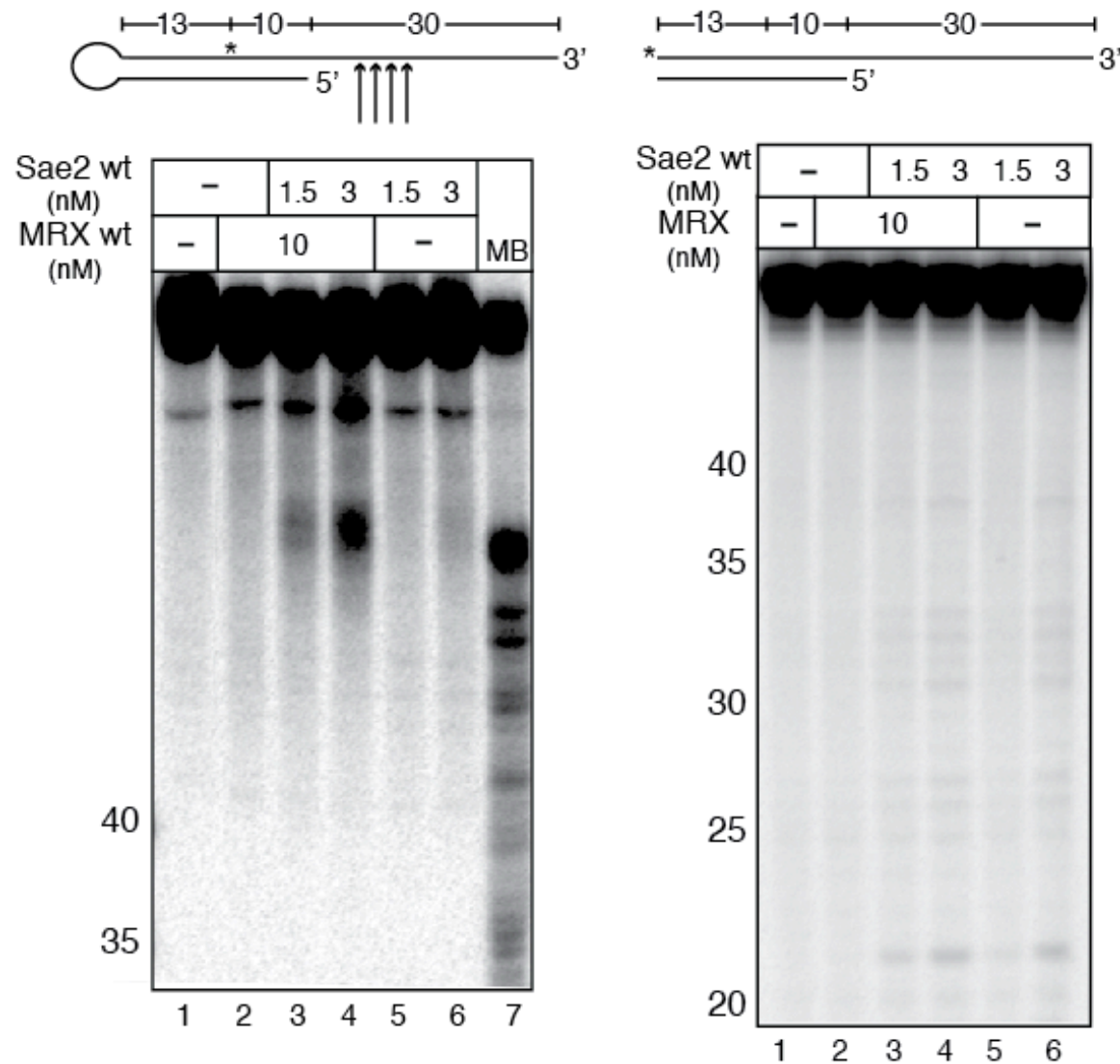
Sae2 exhibits endonuclease activity on hairpin DNA structures:



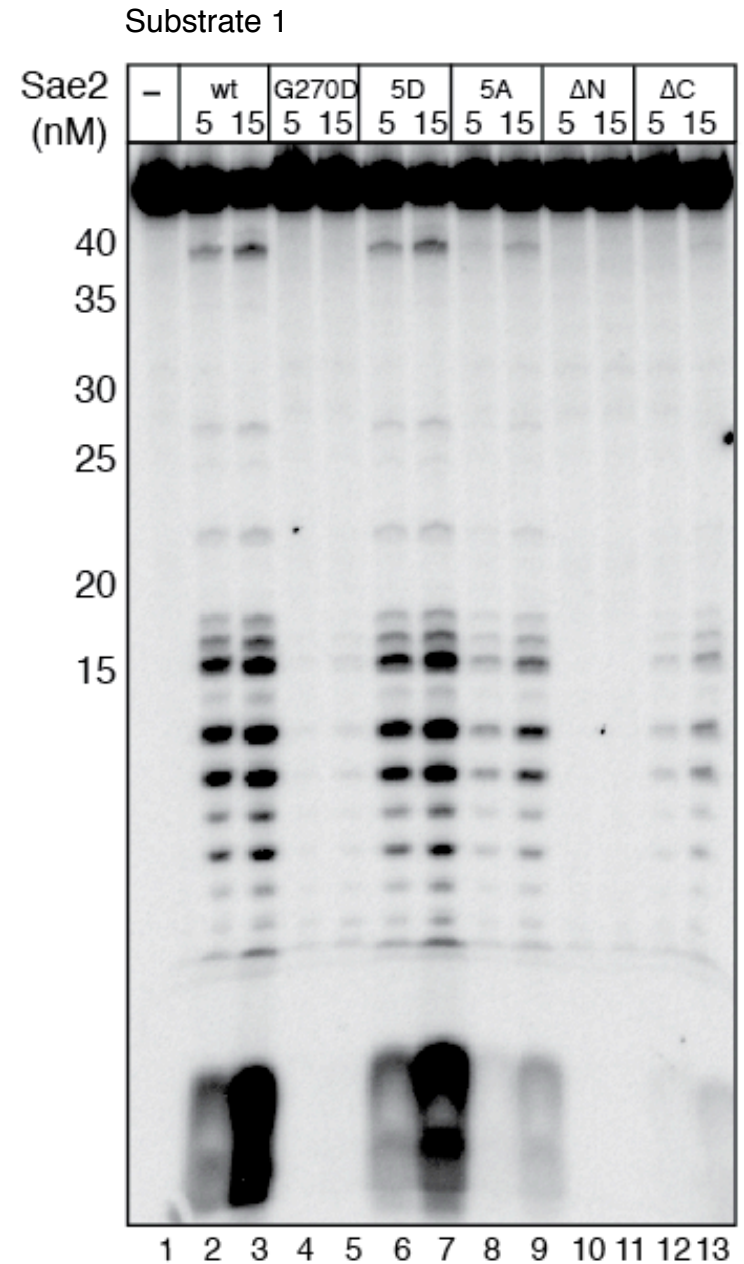
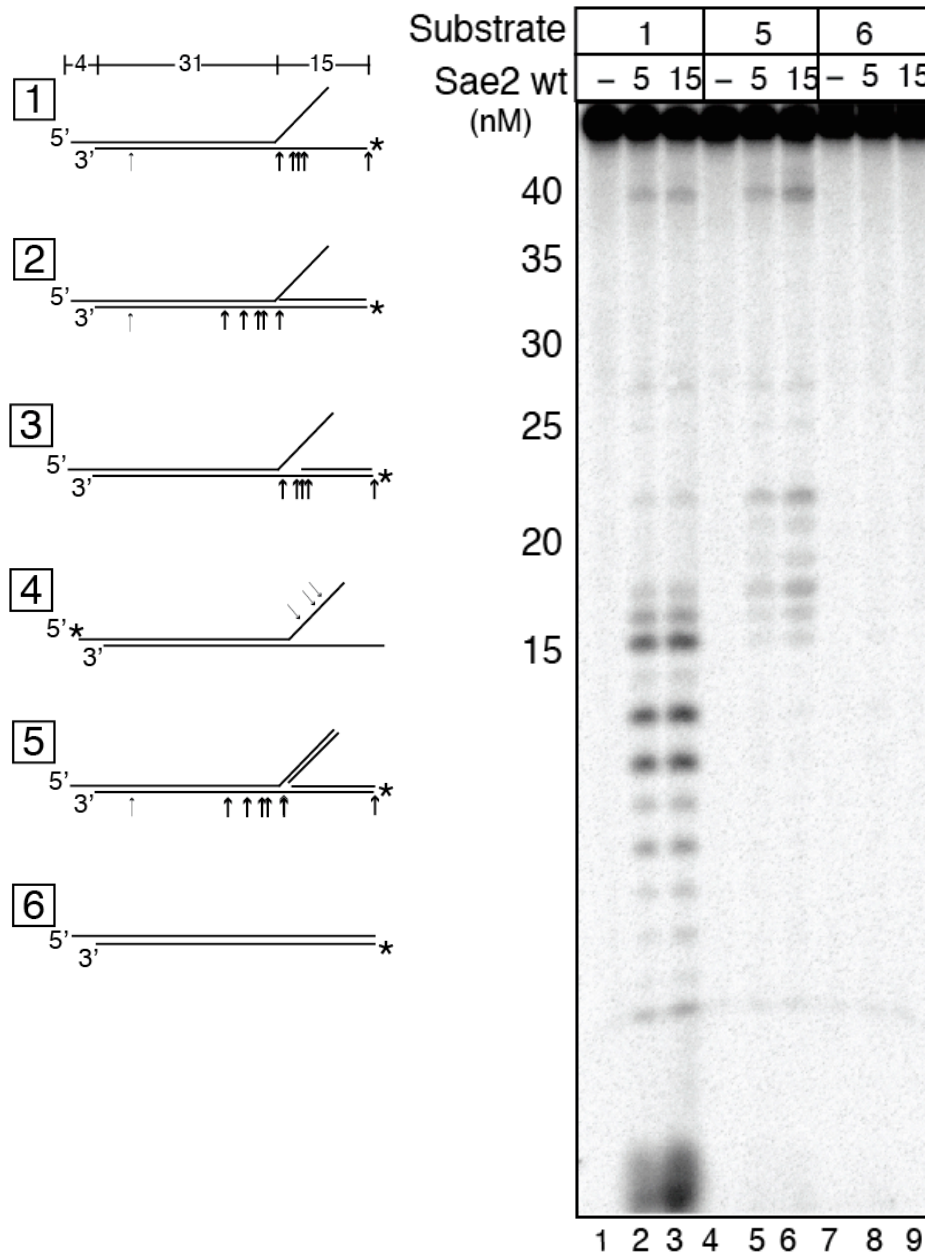
• but the cleavage sites are not at the hairpin tip



At lower levels of [Sae2](#) and MRX, the complexes act cooperatively on hairpin structures:



Sae2 exhibits MRX-independent flap endonuclease activity:



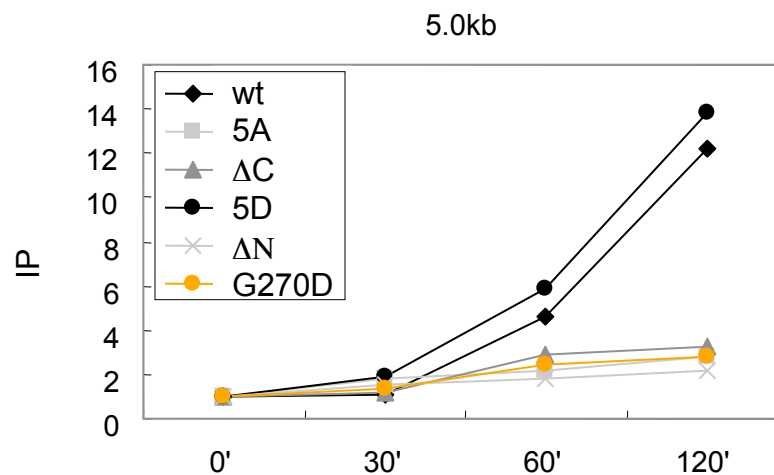
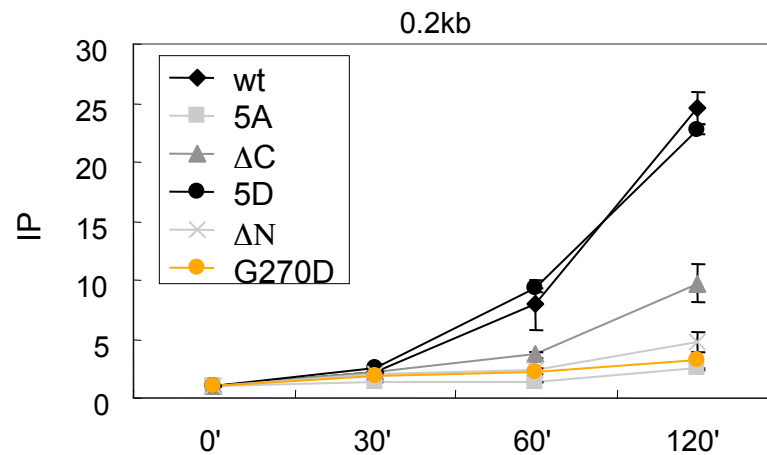
Sae2 mutant phenotypes in resection:



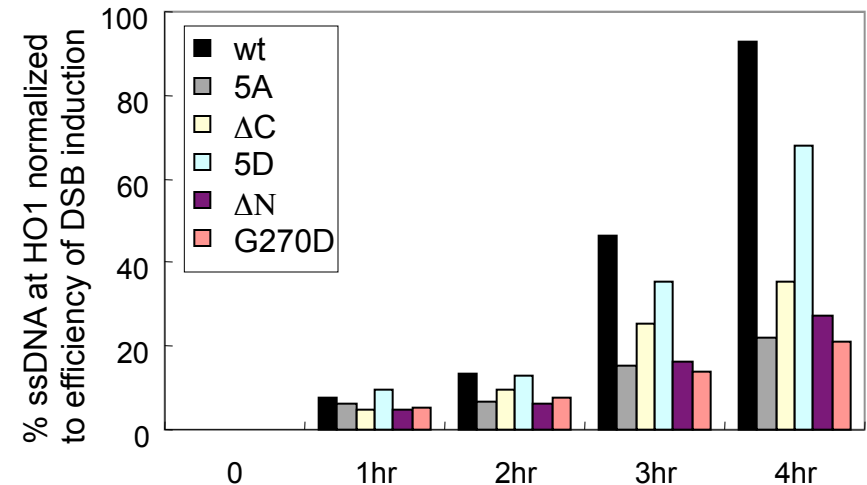
Sang Eun Lee
Kihoon Lee

Univ. of Texas Health Science Center,
San Antonio, TX

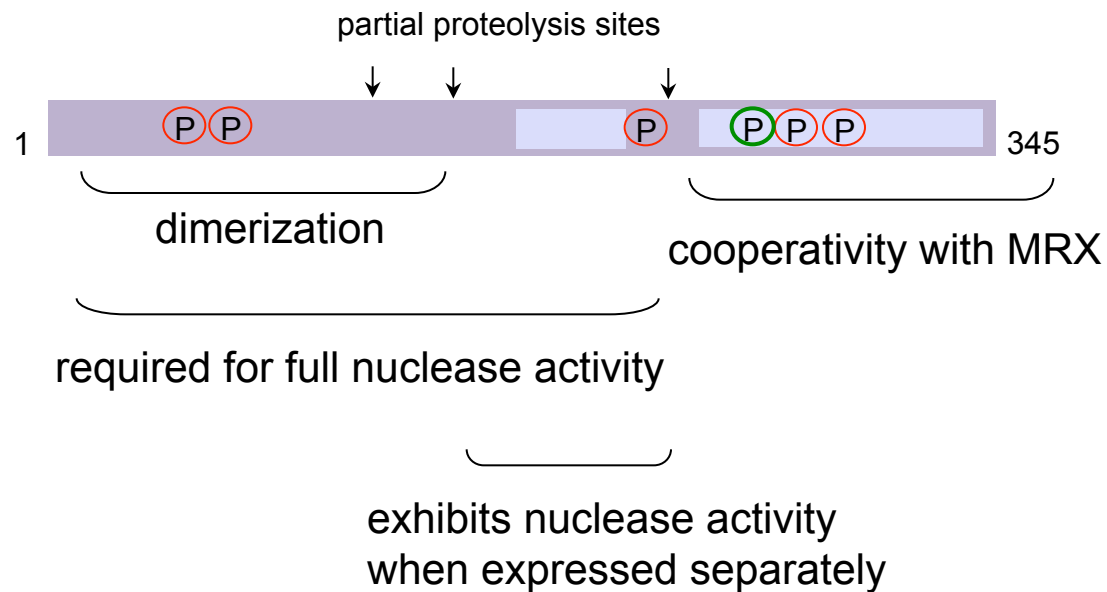
RPA binding to ssDNA (ChIP):



Resection:



summary of Sae2 structure/function analysis:

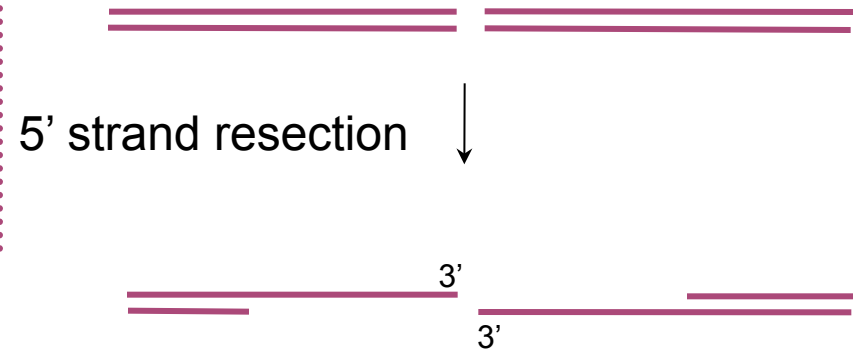


Ⓟ Mec1/Tel1 phosphorylation sites

Ⓟ CDK phosphorylation site

Double-strand break processing in *S. cerevisiae*:

- Mre11/Rad50/Xrs2 (MRX)
- Sae2
- Exo1
- Sgs1(Rmi1/Top3)/Dna2

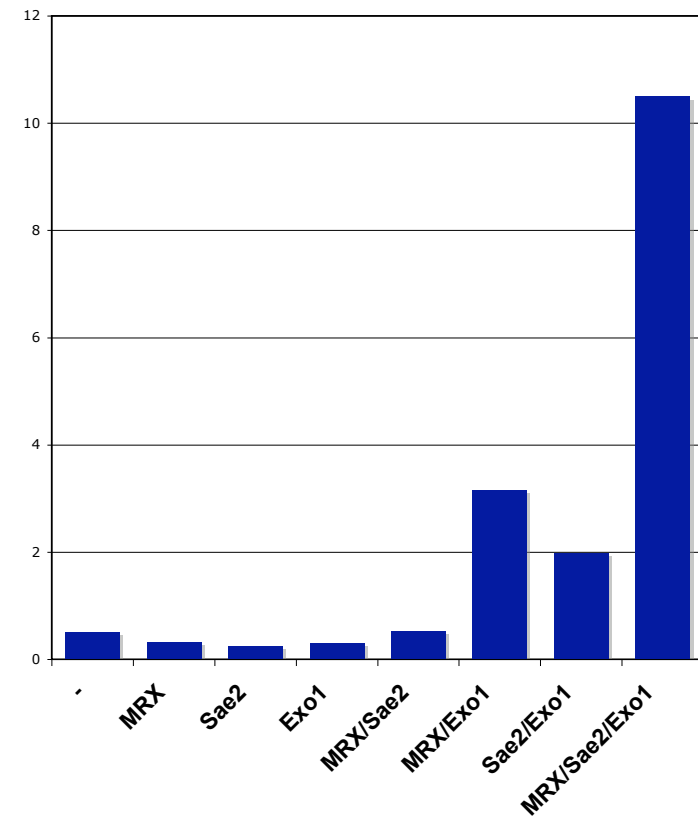
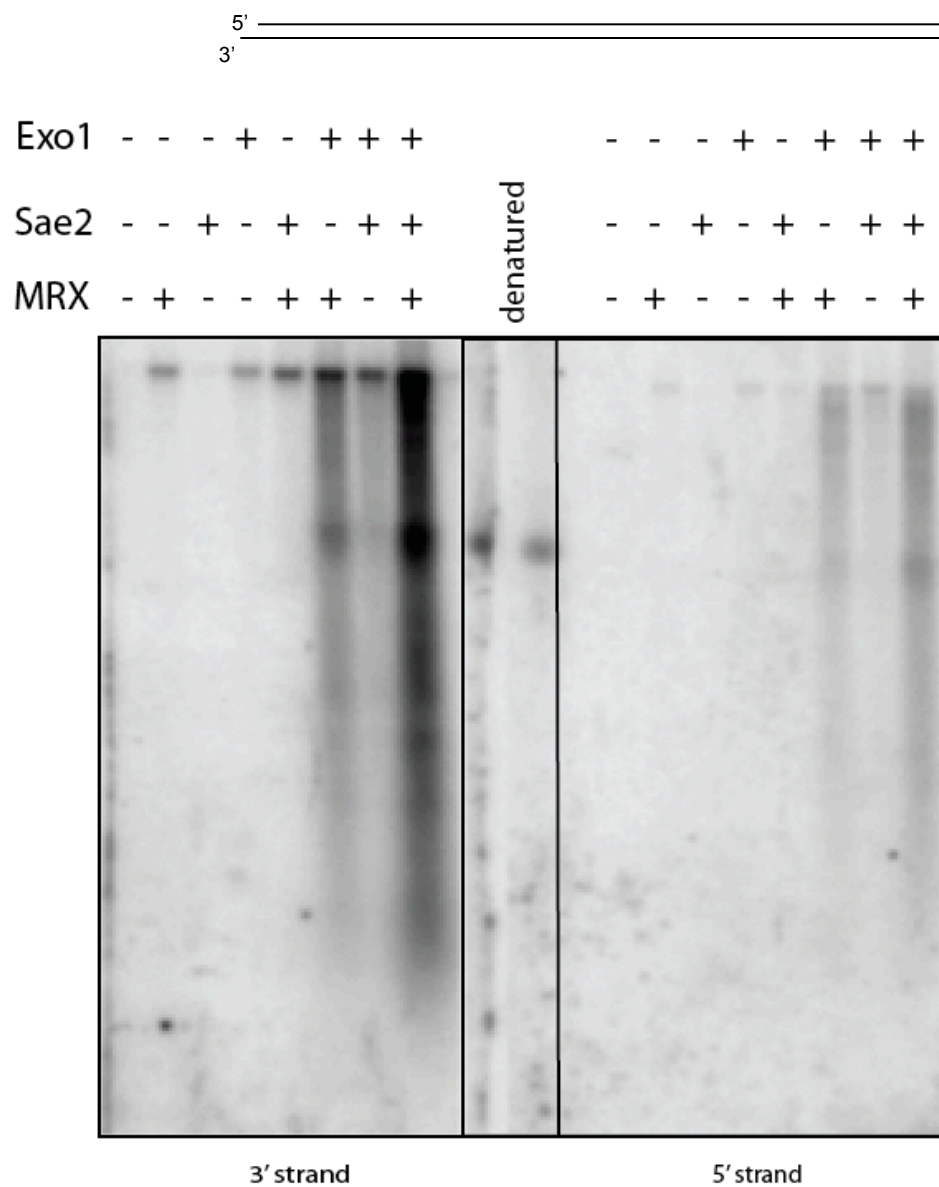


? Which factors are sufficient for 5' strand resection of DSB's?

? Can we demonstrate this with purified components in vitro?

Recombinant yMRX and Sae2 function cooperatively with yExo1 in DNA end processing:

Matthew Nicolette

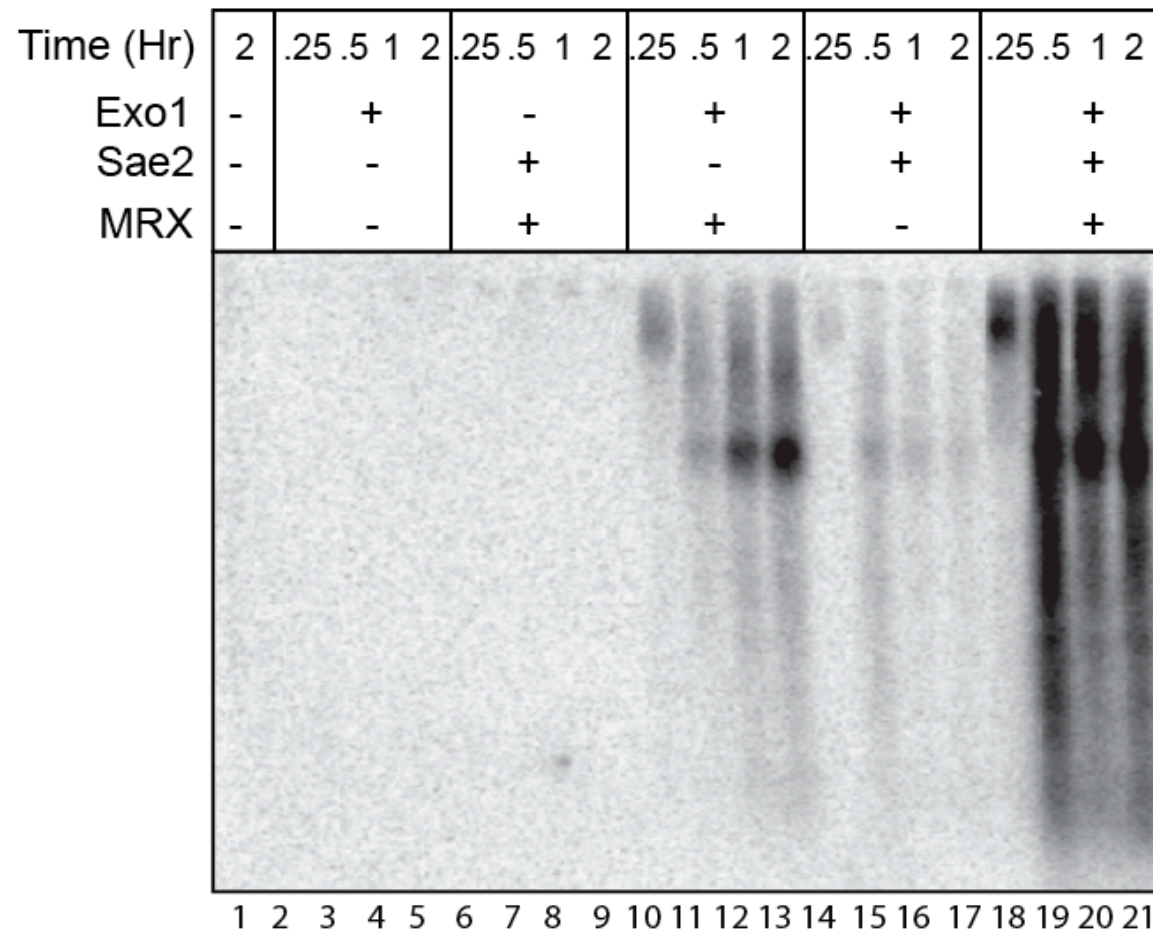


nondenaturing Southern blot with 6.5 kb plasmid DNA linearized substrate, strand-specific RNA probes

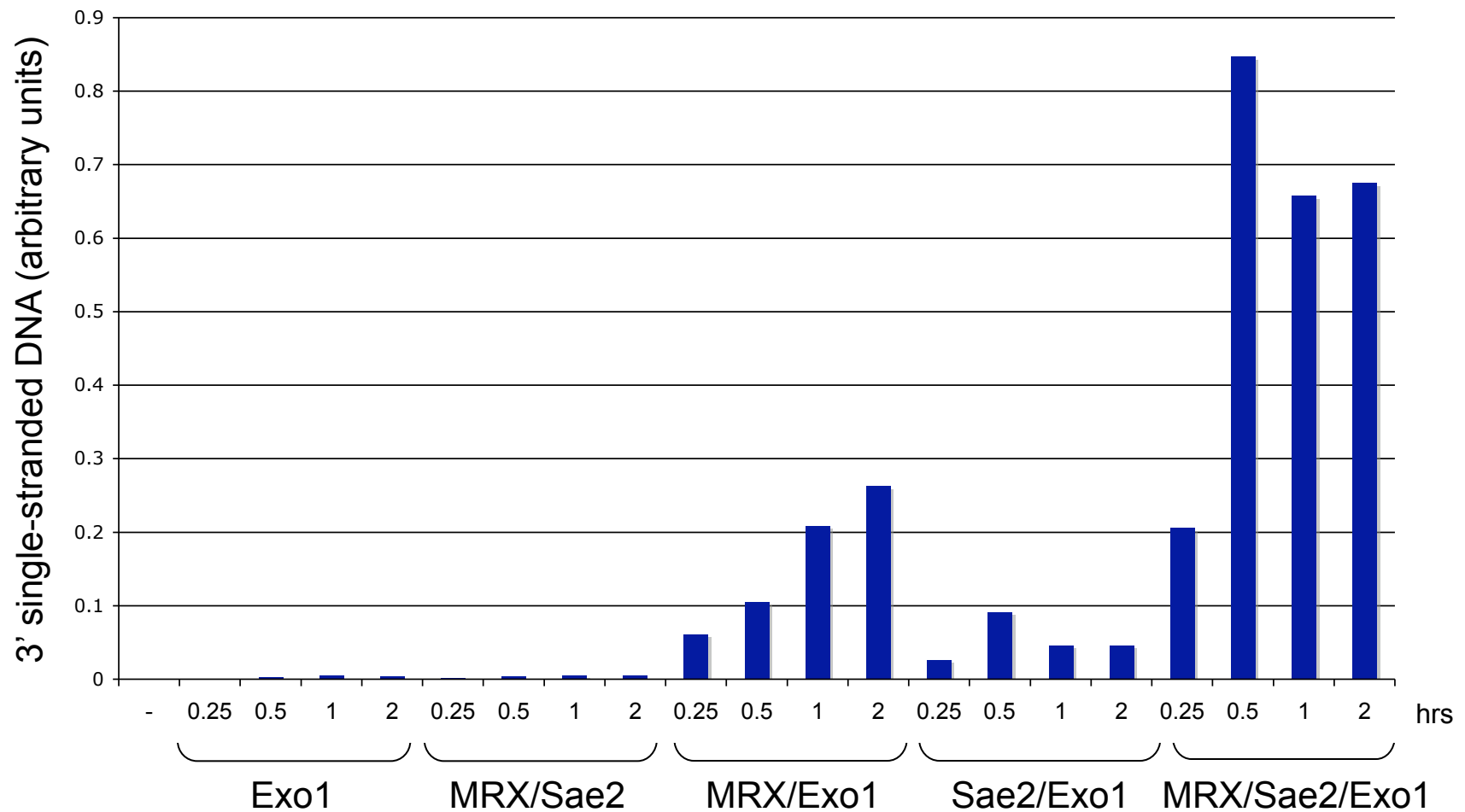
yExo1 acts cooperatively with yMRX and Sae2:



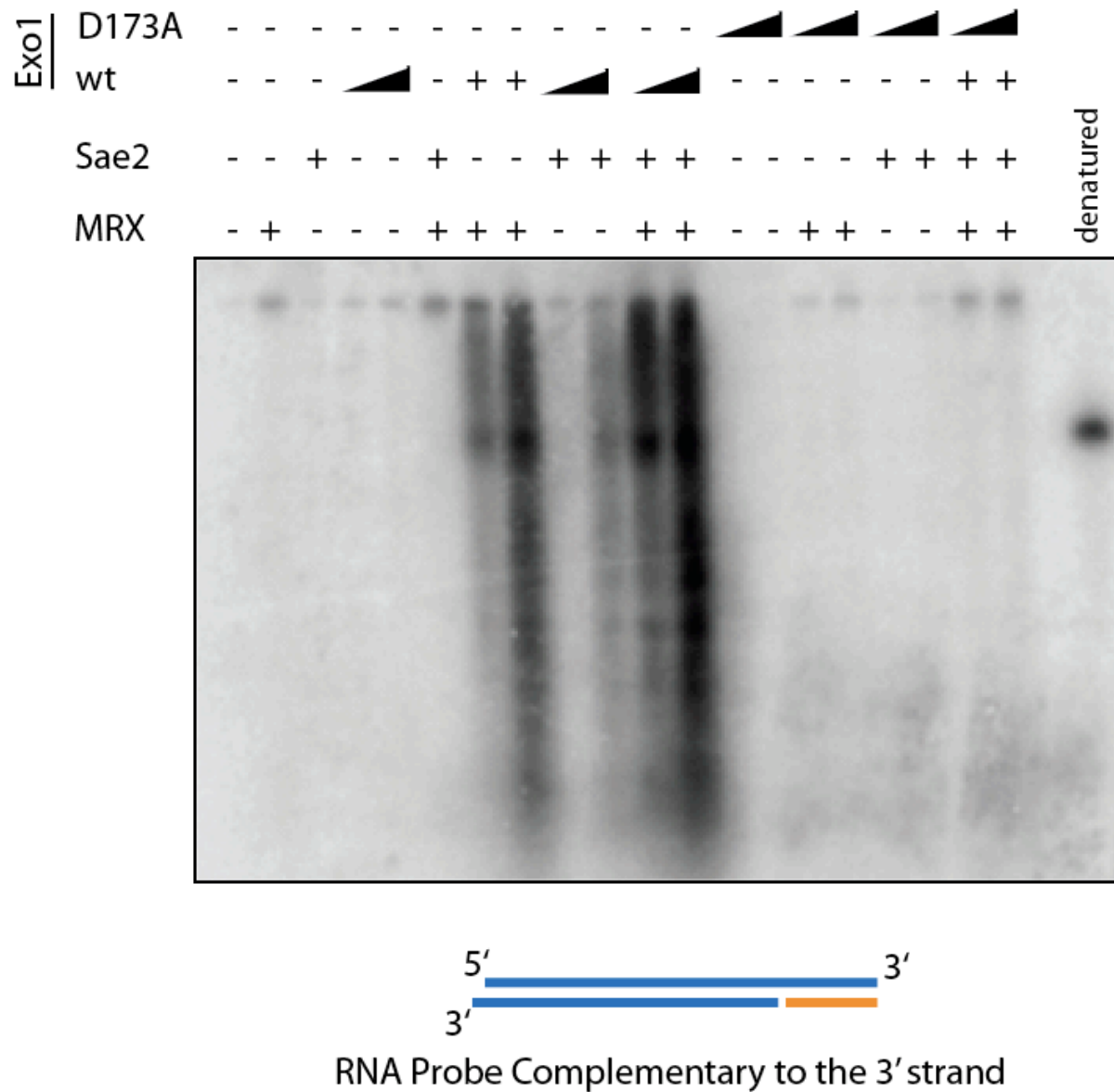
RNA Probe Complementary to the 3' strand



yExo1 acts cooperatively with yMRX and Sae2:



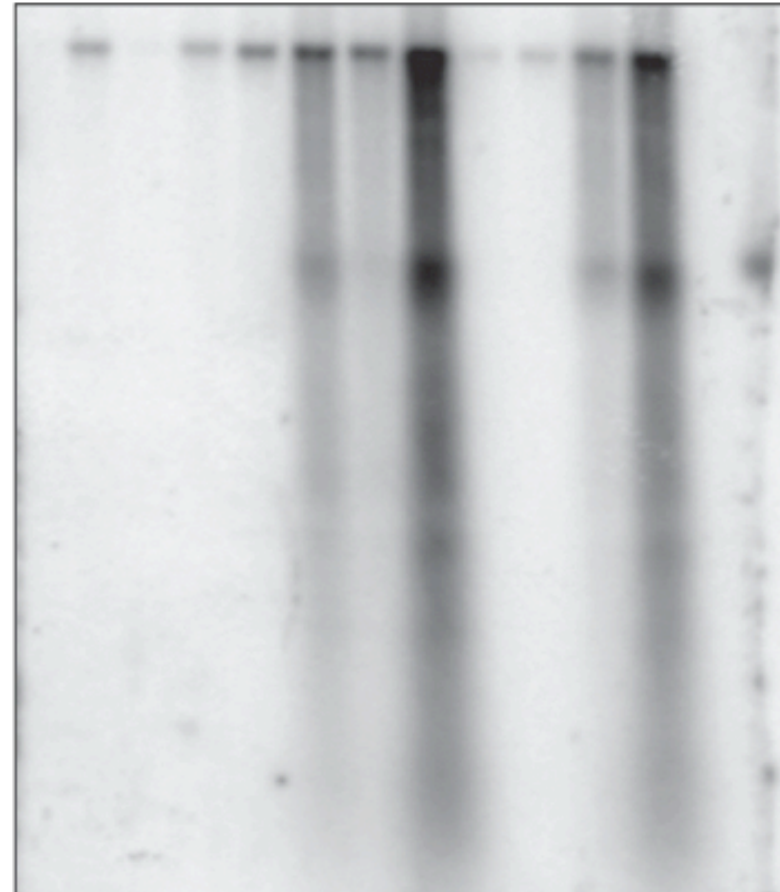
The catalytic activity of yExo1 is responsible for the resection:



Mre11 nuclease activity
contributes only minimally
to resection,

but reduces efficiency
of initial cut that is
dependent on MRX and
Sae2

MRX	Exo1	-	-	-	+	-	+	+	+	-	-	+	+	denatured
	Sae2	-	-	+	-	+	-	+	+	-	+	-	+	
	wt	-	+	-	-	+	+	-	+	-	-	-	-	
	H125N	-	-	-	-	-	-	-	-	+	+	+	+	

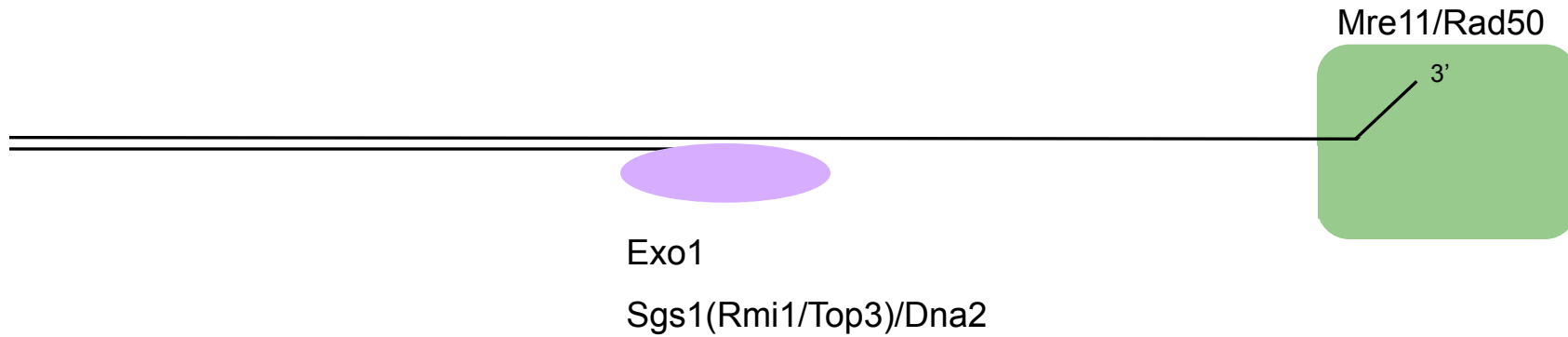


5' ————— 3'

3' ————— ——— 3'

RNA Probe Complementary to the 3' strand

Working model for DSB processing by MRX/Sae2/Exo1:



? Is there a specific DNA structure that is formed by MRX that promotes the entry of or stimulates the catalytic activity of Exo1?

? How is resection controlled through CDK phosphorylation of Sae2?

? What is the function of Mec1/Tel1 phosphorylation of Sae2?

Functional orthologs of Sae2 in higher eukaryotes:

S. cerevisiae Sae2:		267	SPPGFGRLD	FPSTQ	280
human CtIP:	847	TPEN	FW	EVGF	PSTQ 860
Xenopus CtIP:	806	TPEN	FW	EVGF	PSTQ 819
chicken CtIP:	862	TPEN	FW	EVGF	PSTQ 875
C. elegans Sae2/CtIP:	480	TPERY	WDL	TMGPRD	493

- CtIP/Ctp1 in human cells and in *S. pombe* is required for resistance to DNA-damaging agents as well for resection of DSBs and recruitment and activation of ATR

Sartori, A.A., Lukas, C., Coates, J., Mistrik, M., Fu, S., Bartek, J., Baer, R., Lukas, J., and Jackson, S.P. (2007). Human CtIP promotes DNA end resection. *Nature* 450, 509-514.

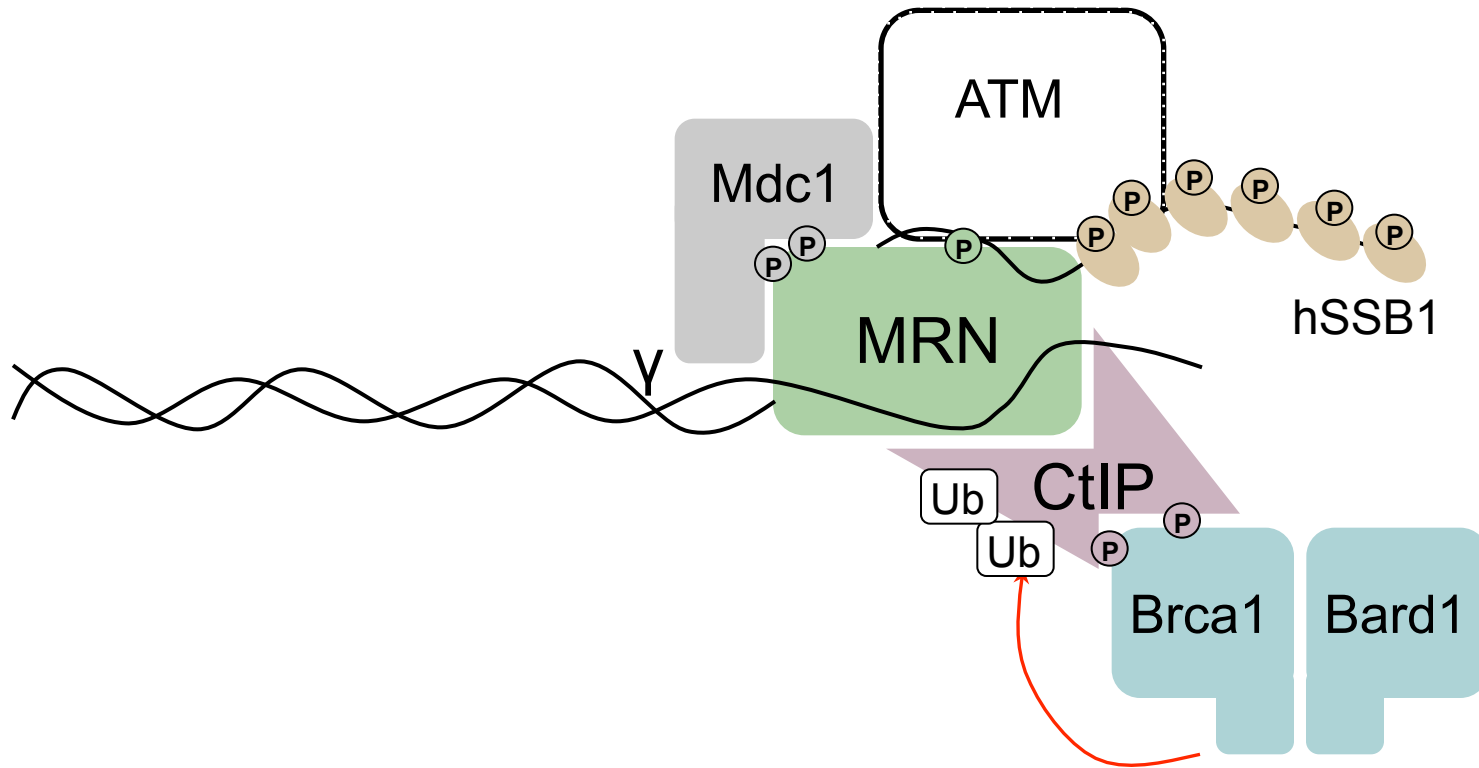
Limbo, O., Chahwan, C., Yamada, Y., de Bruin, R.A., Wittenberg, C., and Russell, P. (2007). Ctp1 is a cell-cycle-regulated protein that functions with Mre11 complex to control double-strand break repair by homologous recombination. *Mol. Cell* 28, 134-146.

- Com1/Sae2/CtIP in *C. elegans* and in *Arabidopsis* is required for meiotic DSB processing and chromosome pairing during meiosis

Penkner, A., Portik-Dobos, Z., Tang, L., Schnabel, R., Novatchkova, M., Jantsch, V., and Loidl, J. (2007). A conserved function for a *Caenorhabditis elegans* Com1/Sae2/CtIP protein homolog in meiotic recombination. *EMBO J* 26, 5071-5082.

Uanschou, C., Siwiec, T., Pedrosa-Harand, A., Kerzendorfer, C., Sanchez-Moran, E., Novatchkova, M., Akimcheva, S., Woglar, A., Klein, F., and Schlogelhofer, P. (2007). A novel plant gene essential for meiosis is related to the human CtIP and the yeast COM1/SAE2 gene. *EMBO J* 26, 5061-5070.

Multiple binding partners of MRN and CtIP at a DSB:



Paull laboratory, UT Austin:

Rajashree Deshpande

Zhi (Jay) Guo

Ben Hopkins

Ji-Hoon Lee

Matt Nicolette

Mingjuan Shen

Elena Sirbu

Soo-Hyun Yang

Xiaoming (Julie) Zhang

(previous):

Bettina Lengsfeld

Venu Bhaskara

National Institutes of Health
Howard Hughes Medical Institute



Sang Eun Lee, Ki-hoon Lee
(Univ. of Texas Health Science Center,
San Antonio, TX)

Allison Rattray, Jeff Strathern (NIH)

